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BRAIN

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Brain

A Journal of Neurology

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BRAIN.

PART 1, VOL. 53.

MICROGLIA: AN EXPERIMENTAL STUDY BY MEANS OF TISSUE CULTURE AND VITAL STAINING.

BY A. Q. WELLS, D.M.OXON.,

AND

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INTRODUCTION.

RECENT progress in histological technique has advanced the knowledge of the cellular structure of the central nervous system, so that the adendritic cells of the brain are now known to be composed of two types of cells, the oligodendroglia and the microglia. In an exhaustive histological study of the microglial elements, Del Rio-Hortega [2] went far to demonstrate that microglial cells are of mesoblastic origin; this contention, however, has its opponents, amongst them being Metz and Spatz [11], who advanced evidence in favour of an ectodermal origin. While acknowledging the work of these histologists, it is apparent that until the origin of microglial cells is definitely established, false conceptions of the pathology of the central nervous system may arise.

The present paper records the results of some experiments performed in an attempt to elucidate the embryological element from which microglia arises. The problem has been attacked by means of tissue culture and vital staining *in vivo* and *in vitro*.

There appears to be comparatively little literature dealing with the cultivation of nervous tissue. In 1907 and 1908 Harrison [5] published his classical work on the development of excised portions of the nervous tissue of the frog after incubation in lymph removed from the lymph-sac. He was able to demonstrate the growth of a fibre from these cells which was in many ways similar to a neurone. More recently Mossa [12] has shown that if isolated embryonic spinal root ganglia are incubated in a suitable medium, outgrowths take place which closely resemble nerve-fibres. None of these workers have, to our knowledge, attempted to recognize the cellular elements in their cultures by means of the selective silver impregnation methods of staining, and many of their conclusions must consequently be conjectural.

MATERIAL AND METHODS.

Material.—Cultures were made from the central nervous system of fowl embryos of from three to twenty-one days' incubation. Great care was necessary to rid the implant of overlying mesoblastic tissue and at the same time to avoid any considerable damage to the nervous tissue. Cultures showing outgrowths of fibroblastic tissue were immediately discarded. After repeated experiments it was found that the area of the pons and medulla was the most easily isolated. Dissection was carried out by means of needles and a binocular dissecting microscope.

Cultures were also made from periosteum, limb bud and retina for comparison with those derived from nervous tissue.

Culture technique.—Cultures were made in both solid and fluid media, by the usual coverslip technique [14]. Owing to the great delicacy of the retina, transplantation in solid medium was found to be impracticable. It was therefore grown in fluid medium only.

The solid medium employed was one drop of fowl embryo extract, diluted with Pannett's isotonic salt solution, mixed with one drop of fowl plasma. The cultures were changed to fresh medium every forty-eight hours.

The fluid medium consisted of the fluid expressed from the clot resulting from the addition of twenty drops of fowl plasma to thirty drops of embryo extract. One drop of this fluid was placed on the coverslip with the piece of tissue to be cultured, and the whole sealed off in the usual way. The culture was washed every forty-eight hours with embryo extract and a fresh drop of medium applied.

Vital staining technique.—In the experiments with vital staining *in vitro*, neutral-red and trypan-blue were used. The neutral-red was exhibited by substituting 0·5 c.c. of a 0·1 per cent. solution of neutral-red for 0·5 c.c. of distilled water in making up 25 c.c. of Pannett's solution. This fluid was used as a diluent for the embryo extract. In this dilution, about 1 in 100,000 in the final medium, no toxic effects upon the culture were observed. The trypan-blue was exhibited by substituting 2·5 c.c. of a 1 per cent. solution of trypan-blue for 2·5 c.c of distilled water in making up 25 c.c. of Pannett's solution, giving a dilution of about 1 in 2,000.

The technique for the vital staining *in vivo* is given later.

Histological technique.—The cultures were placed in formol bromide, a 10 per cent. solution of formaldehyde (Merck's specific gravity 33) made up with 4 per cent. ammonium bromide solution. This solution was faintly acid. Fluids with a neutral or alkaline reaction to litmus were found less reliable. At the end of twenty-four hours in a second bath, they were placed in another bath of formol bromide and kept at a temperature of 37° C. for one hour. From this they were transferred without washing into a dish containing 25 c.c. of distilled water and two drops of ammonia, where they remained for a period of twenty to thirty minutes. From this, without washing, they were placed in a silver bath made up as follows: to 5 c.c. of a solution of 10 per cent. silver nitrate were added 20 c.c. of a 5 per cent. solution of sodium carbonate. Ammonia was then added drop by drop until the precipitate just disappeared, leaving a colourless and odourless fluid; 50 c.c. of distilled water were then added. The cultures were retained in this silver bath at a temperature of 37° C. for a period of not longer than fifteen minutes. They were then very rapidly washed in distilled water and placed in a bath of 1 per cent. formalin in distilled water; while in this bath the coverslips were kept on the move either by rocking or actually holding them in forceps and waving them to and fro in the bath. As soon as they ceased to cloud the bath or to become more brown they were transferred without washing into a bath of gold chloride (5 c.c. of a 1 per cent. solution of gold chloride to 25 c.c. of distilled water). In this they were left until the culture had become a dirty grey colour, when they were placed in a bath of 5 per cent. hyposulphite of soda. At the end of five minutes they were washed in several changes of distilled water, passed through the alcohols into xylol and mounted in Canada balsam. Several were also stained for fat with Scharlach R. and mounted in glycerine jelly. By these methods permanent specimens were obtained. As controls, frozen sections from adult tissue were found to stain admirably and selectively for microglia by these methods.

MICROSCOPICAL EXAMINATION.

Histological appearances of tissues before explantation.—Pieces of the embryonic fowl brain chosen for cultivation were fixed, cut and stained by the method described. Blood-vessels were observed within the brain substance. This was of significance as showing the presence of mesoblastic elements in the cultures. As this paper is not concerned with the other cells of the central nervous system, these will not be described.

Serial sections through the eye of the embryonic fowl were cut and stained by routine methods. Careful examination of the retina failed to reveal any blood-vessels within its substance. This fact was made use of in obtaining a pure culture of ectodermal tissue.

Observations on the living cells in vitro.—In the living brain cultures three main types of cells were seen: (1) A cell with a long process which grew out rapidly to cells already lying away from the implant; the processes from several such cells tended to become associated, and at their termination to spread out fanwise in very fine ultimate strands. (2) A small cell with an oval nucleus, having usually three, but occasionally two, cytoplasmic processes. Cells of this type were intermingled with those of the previous type at the plaque-like edge of the implant. (3) A round cell with an oval or slightly irregular nucleus. Cells of this form were distinguishable by the end of the first day's growth *in vitro*.

The present communication deals with the third type of cell only. The writers hope to discuss the possible nature of the other two types in a later paper.

The cell Type No. 3 was found in all cultures. It was actively motile, and in many cultures migrated a considerable distance from the implant edge. This was more marked when the culture medium was fluid. Further, in fluid medium these cells appeared to flatten themselves out on the coverslip, so that they had the appearance of being larger and of having a less dense nucleus than those in solid medium.

In cultures of three days' duration in solid medium, a definite change in the character of the cells was noted. They lost their round shape and became elongated and irregular in outline, whilst some protruded thick processes branching out in all directions. The nuclei at this stage were also elongated or irregular in shape.

Between the third and sixth days of cultivation *in vitro* more interesting changes were observed. The cells were seen to grow out into the medium in a series of chains, each cell being an independent unit and having the characteristics of the cells seen at the end of three days. During this period of growth mitotic figures were commonly seen. Towards the sixth day the cells tended to become more isolated, and there was less evidence of chain formation. At the same time, the cells ceased to be elongated and assumed an even more irregular shape with one or two long, fine processes passing centrifugally from the centre of the culture. Cells of this type were present in the cultures up to the twenty-first day of cultivation.

After six days' growth some of these cells showed degenerative changes. These cells became rounder, with shorter processes, or in some cases with none at all. The protoplasm contained many small refractile granules, and the nucleus had become oval. Cultures in fluid medium showed more cells with degenerative changes than those in solid medium.

Observations were made by means of the dark-ground illumination method described by Strangeways and Canti [15]. Remarkable activity was observed in the cells. Protoplasmic protrusions were constantly thrown out and then withdrawn. Mitochondria and cell granules were in constant violent movement. Highly refractile fat droplets were present in varying amounts. The appearance and behaviour of the cells were exactly similar to those noted by Fell and Andrews [3] in the wandering cells of rat sarcoma.

Cultures of eight days' duration were chosen for vital staining. These were examined at frequent intervals under the microscope in a hot box at a temperature of 37° C. The neutral-red culture showed staining of the cell granules beginning about fifteen minutes after the commencement of cultivation. The granules were of varying size and scattered throughout the cell, but the largest number were seen round the nucleus. The staining increased in intensity up to forty-eight hours, when a maximum appeared to have been reached. The trypan-blue cultures did not show any dye in the cell for at least twenty-four hours after the commencement of cultivation. The granules of dye varied in size, but were smaller than the granules stained with neutral-red. They were scattered throughout the cell and were not especially congregated round the nucleus. The amount of dye in the cell increased up to ninety-six hours of cultivation.

In the cultures of periosteum and limb bud, cells entirely similar to those described were found. Their behaviour with vital dyes was strictly comparable.

The retinal cultures, whilst showing a good area of outgrowth, produced no cells of the Type 3 described in the brain cultures. The significance of this will be discussed later.

Observations on the cells after fixation.—The cells under consideration showed the typical staining reactions, after silver impregnation, which are seen in microglial cells. The nucleus had a fairly dense chromatin network. In cultures of three days' duration, or more, the protoplasm had a dirty grey colour after silver impregnation, and there were a few dense black granules within the protoplasm. In places these minute dark granules appeared to be on the surface of the cell. The processes showed up well and closely resembled those seen in microglia from adult brain tissue.

The cells showing degenerative changes after six or more days' cultivation *in vitro* showed many small granules which stained well with Scharlach R.

The cells from the periosteum and limb bud cultures showed a very striking resemblance to those found in the brain cultures. Their form was entirely similar and they showed the typical staining reactions after silver impregnation.

Intravital staining experiments in vivo.—The literature on this subject is somewhat scanty, and the following is a review of the main works. Goldman [4], by using large intravenous doses of trypan-blue, was able to demonstrate a diffuse staining of the lepto-meninges: no certain staining of the neuroglial elements was observed. Woollard [16] injected the dye into the subarachnoid space and demonstrated the dye in the lepto-meninges and in the mesothelial cells lining the perivascular spaces which surrounded the entering vessels of the spinal cord and brain. In none of these experiments did the nerve, ependymal or neuroglial cells contain elements of dye. He repeated these experiments, adding laked blood-corpuscles to the trypan solution, so as to cause irritation of the lepto-meninges: the results in no way differed from those obtained in his previous experiments. MacCurdy and Evans [8] reported the staining of the glial nuclei and "Gitterzellen" in animals suffering from experimentally produced poliomyelitis or polio-encephalitis. After damaging the brain by puncture wounds, Macklin and Macklin [9] injected trypan-blue and demonstrated the presence of the dye in macrophages around the wound. More recently this work has been repeated by Russell [13], who has shown that the microglial cells in the vicinity of such a wound contain particles of trypan-blue; in the microglial cells situated farthest from the wound only one or two small granules were present, while in the active swollen microglial cells in the immediate vicinity of the wound there was considerably more dye. She assumed from this evidence that microglial cells were probably of mesodermal origin, as suggested by Del Rio-Hortega. Kubie [6], using the supravital technique, was able to stain the perivascular tissues of the central nervous system: but he was unable conclusively to demonstrate the presence of the dye within microglial cells. In a review of the whole subject of vital staining, Capell [1] concludes that the dyes do not pass into brain tissue and are not taken up by any of the essential elements of the neuraxis except the lepto-meninges, choroid plexus and perivascular tissues. In spite of this apparent protection of the nervous tissues to vital dyes it was decided to carry out the following series of experiments.

Four rabbits were given intravenously a daily injection of 1 per cent. trypan-blue in distilled water. The injection varied from 5 to 10 c.c. At the end of ten days two rabbits, and at the end of fourteen days two others, were killed by ether anæsthesia. The brain was immediately dissected out and placed in formol-bromide. After two days hardening, frozen sections were made and stained by the method described at the beginning of this paper. Pieces of brain were also embedded in paraffin, cut and stained with a weak solution of carmine.

On microscopical examination the sections stained by means of the silver impregnation method proved of little value, as the colour produced by the silver staining and that of trypan-blue were impossible to separate. However, the microglial cells showed evidence of alteration from normal: the cells were larger, and had fewer fine processes. In other words, they resembled the stage when microglial cells are beginning to react in the neighbourhood of a wound. The sections stained with carmine were of considerable interest. In those rabbits which had received intravenous trypan-blue for a short period, there was a diffuse slight bluish tinge of the whole brain, but in the region of the hippocampus a more intense blue colour was present. Under the microscope the nerve-cells were found to have taken on a faint blue tinge: careful scrutiny failed to reveal granules of stain within the cell, and it was certain that the staining was not associated in particular with the Nissl bodies. The microglial cells that were approximated to the nerve-cells showed in more than one place the presence of blue pigment lying around the nucleus. The granules were small and difficult to observe unless care was taken. In the region of the hypothalamus microglial cells appeared to be more numerous and to contain blue granules. These microglial cells were situated in close proximity to blood-vessels. Their situation is of importance, as Kubie has shown that the monocytes in the region of the cerebral blood-vessels will take up neutral-red: it is, therefore, possible that these cells observed close to blood-vessels may have been monocytes derived from the vascular system.

In the brains of the rabbits that had been injected intravenously for a longer period, the presence of granules in microglial cells was strikingly seen.

To the naked eye the brains were stained a deep blue, especially in the region of Ammon's horn. Microscopically a large proportion of the cells which could be recognized as microglial were crowded with trypan-blue. Microglial cells which were satellites to neuronic cells were particularly rich in the dye: the dye was scattered throughout the fine processes of the cells, and at times was collected chiefly around the nucelus. This was especially noticeable in the regions of the basal ganglia, thalamus and Ammon's horn. The microglial cells in the cortex itself contained as a whole less dye, and many cells no dye at all. In the white matter throughout the brain many microglial cells lying away from any recognizable blood-vessel contained particles of the dye.

Scrutiny of the other nervous elements, such as the nerve-cells and neuroglial cells, failed to reveal the presence of particles of trypan-blue within their substance. However, cells in the perivascular tissues contained many particles, as did also the cells of the choroid plexus; the former cells are probably similar to the cells stained by neutral-red, as reported by Kubie.

From these experiments it was clear that microglial cells will take up particles of trypan-blue, provided the trypan-blue is supplied in sufficient quantities and concentration.

DISCUSSION.

Cultures of embryonic brain have shown the presence of a cell which has many of the characteristics of microglial cells of adult tissue. This type of cell has the following resemblances to normal microglia:—

(1) A selective affinity for silver after the impregnation methods of Del Rio-Hortega.
(2) An irregular outline, with many processes, some of which are of the fine wire type.
(3) A nucleus of similar shape.
(4) Similar distribution of chromatin within the nucleus.
(5) The presence of fine dark granules in the protoplasm after silver impregnation.

We felt justified, therefore, in concluding that these cells were microglial cells.

The striking resemblance between the cells in the brain cultures and the wandering cells in the cultures of periosteum and limb bud suggested that these two types were identical. The wandering cells belong to the reticulo-endothelial system, and have been carefully described by Maximov [10], Lewis [7] and others. They are also known as histio-

PLATE I.

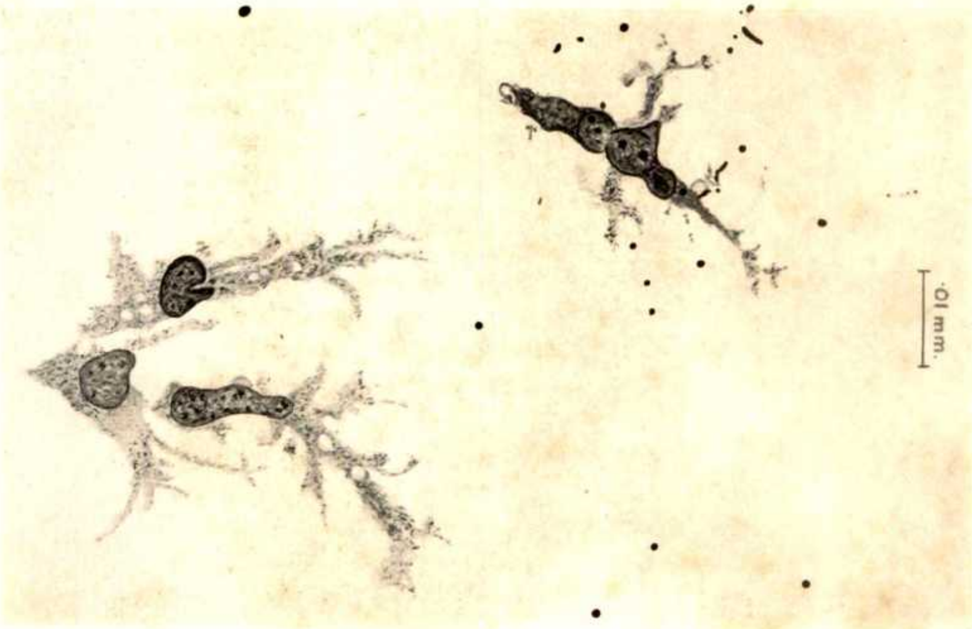

FIG. 1.

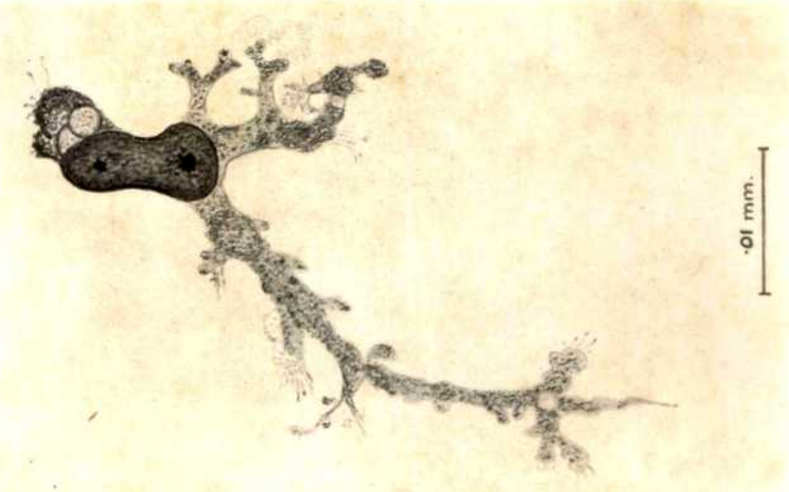

FIG. 2.

To illustrate paper by A. Q. Wells and E. Arnold Carmichael.

PLATE II.

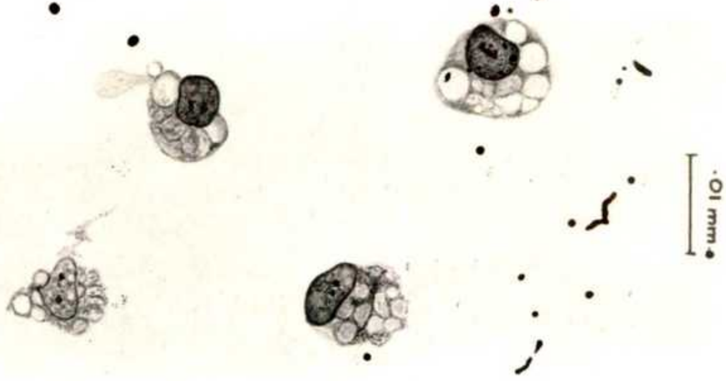

FIG. 3.

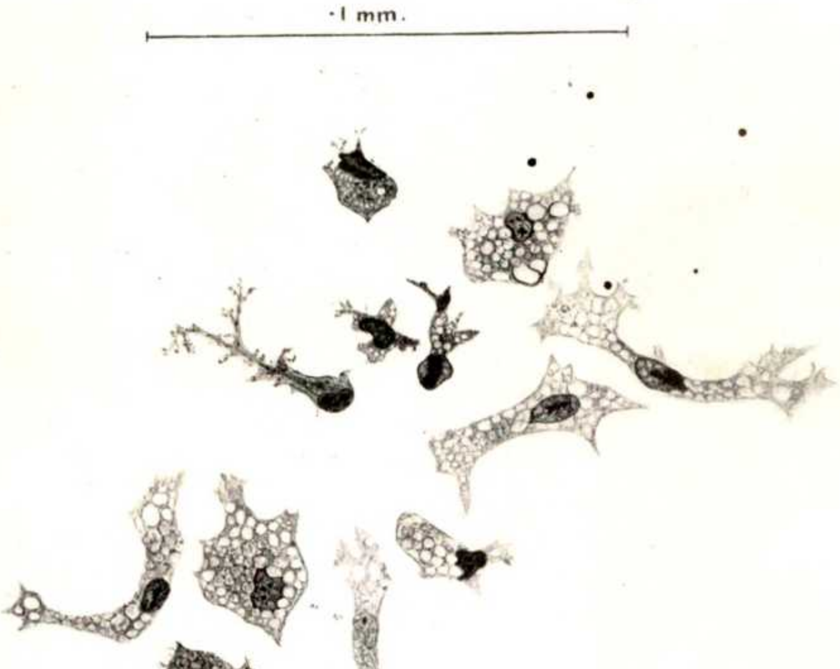

FIG. 4.

To illustrate paper by A. Q. Wells and E. Arnold Carmichael

PLATE III.

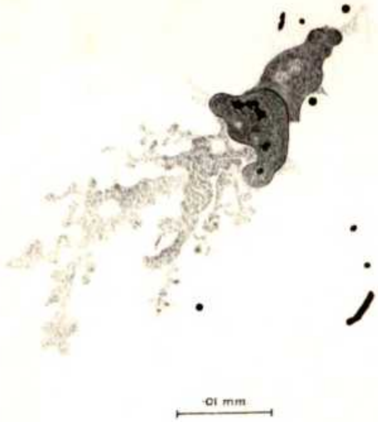

FIG. 5.

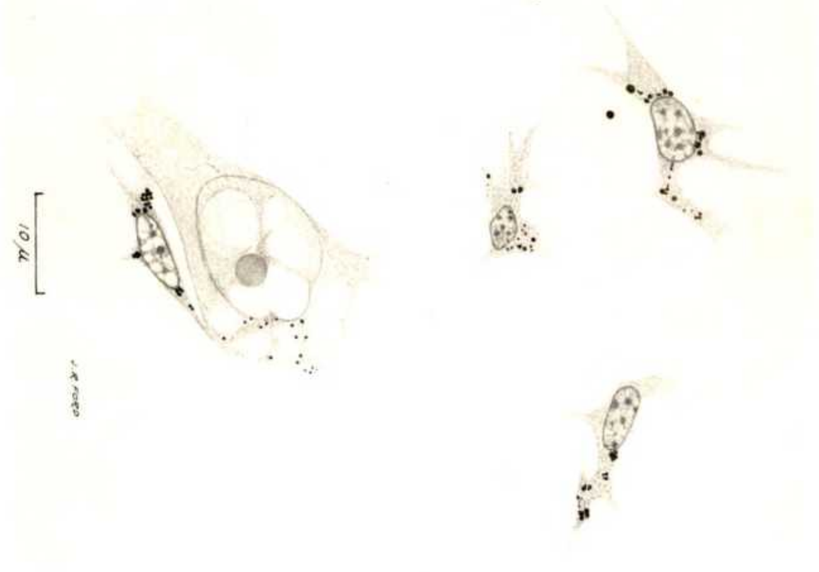

FIG. 6.

To illustrate paper by A. Q. Wells and E. Arnold Carmichael.

cytes and macrophages. They are of mesoblastic origin; they must arise from the blood-vessels, which, as has already been noted, were also present in the substance of the brain explanted.

The next step was to find some tissue that was definitely free from mesoblast. To obtain embryonic brain so early that blood-vessels had not formed, and at the same time to free it from the overlying mesoblast, was found to be impracticable. For this reason the purely ectodermal embryonic retina was used. As stated above, cultures from retina showed a complete absence of microglia-like cells. While recognizing that this was by no means a conclusive proof of the mesoblastic origin of microglia, it may be considered an additional fact in favour of such a conclusion.

The wandering cells of the reticulo-endothelial system have a definite affinity for the vital dyes. The series of experiments with neutral-red and trypan-blue showed that the cells cultivated from brain had the same affinity. The distribution of neutral-red within the cell was exactly similar to that described by other workers as occurring in wandering cells.

Finally, if it could be shown that normal microglia in adult brain also took up these vital dyes *in vivo*, the chain of evidence in favour of their mesoblastic origin seemed complete. As already described, experiments with trypan-blue *in vivo* showed that microglia has the faculty of ingesting the dye.

CONCLUSIONS.

1) Microglia is of mesoblastic origin, and is analogous to the resting histocytes or fixed macrophages of the reticulo-endothelial system.

(2) Microglia is probably a part of the reticulo-endothelial system.

SUMMARY OF RESULTS.

(1) Fragments of brain from embryonic fowl of from three to twenty-one days' incubation were cultivated *in vitro* for from one to twenty-one days. These cultures showed cells closely resembling microglia.

(2) These cells showed characteristic staining with silver impregnation methods.

(3) Cultures from embryonic periosteum and limb bud showed exactly similar cells.

(4) Cultures from embryonic retina showed no such cells.

(5) These cells reacted to vital dyes *in vitro* in the same way as do wandering cells.

(6) Microglial cells showed phagocytic properties to trypan-blue *in vivo.*

It is a pleasure to us to express our thanks to Miss Fell, Director of the Strangeways Research Laboratory, for much help in practical details and for stimulating suggestions. We also wish to thank Professor Fraser for constant encouragement and helpful criticism. One of us (E.A.C.) carried out this work with the aid of a grant from the Medical Research Council.

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DESCRIPTION OF PLATES.

Fig. 1.—Cells from a culture of 16-day embryonic chick brain. Note the irregular-shaped nucleus and many branched processes. The resemblance to microglial cells of adult tissue is apparent.

Culture medium: Fowl plasma and embryo extract. 7 days' growth. Hortega impregnation method.

Fig. 2.—Cell from a culture of 16-day embryonic chick brain. The cell has an irregular-shaped nucleus and many branched processes and closely resembles a microglial cell of adult tissue.

Culture medium: Fowl plasma and embryo extract. 7 days' growth. Hortega impregnation method.

Fig. 3.—Cells from a culture of 5-day embryonic chick brain. These cells are round with irregular-shaped nucleus and contain globules of fat. They resemble the compound granular cells.

Culture medium: Fowl plasma and embryo extract. 18 days' growth. Hortega impregnation method.

Fig. 4.—Cells from a culture of 4-day embryonic chick periosteum. These cells have irregular-shaped nuclei and processes branched in varying degrees.

Culture medium: Fowl plasma and embryo extract. 21 days' growth. Hortega impregnation method.

Fig. 5.—Cell from a culture of 4-day embryonic chick periosteum. Note the irregular-shaped nucleus and many branched processes. This cell is very similar to an adult microglial cell.

Culture medium: Fowl plasma and embryo extract. 21 days' growth. Hortega impregnation method.

Fig. 6.—A drawing of microglial cells from the brain of a rabbit injected intravenously with trypan-blue. The upper three cells are from the region of the white matter; the lower cell is a satellite to a neuronic cell. Note the particles of trypan-blue in the processes and around the nucleus of the microglial cells.

Alum carmine stain.

SPINAL SYMPTOMS IN CHLOROMA AND LEUKÆMIA.

BY MACDONALD CRITCHLEY AND J. GODWIN GREENFIELD.

(From the Pathological Laboratory, The National Hospital, London.)

IN contradistinction to the cerebral manifestations of the severe disorders of the blood-forming organs, symptoms of a paraplegic kind have received comparatively scant attention in the literature. Although rarely mentioned, these spinal forms are not actually uncommon. Failure to recognize the importance of this association of neurological and constitutional symptoms has in part accounted for the incorrect diagnosis of the great majority during life. Again, the varied guise under which the paraplegia may appear has added to the difficulties.

Special problems arise in connection with certain of the spinal changes in the leucoses which, despite their rarity, may nevertheless throw light upon the causation of the commoner paraplegic manifestations of pernicious anæmia.

Among the contributions of note, certain stand out in importance. Such are to be found in Bassoe's article (1918) [1] and in Heissen's paper [13] on Chloroma and the Nervous System published in 1925. Two years later Holmes delivered an address to the meeting of the Association of Physicians, on the neurological aspects of leukæmia and chloroma, but his paper has never been published.

Some of the earliest references to the subject are of purely clinical nature and it is difficult to assign such cases to their correct category. Mosler's case [23] is illustrative of this point; in a very brief note he gives details of a clinical case of a man, aged 35, suffering from splenic anæmia accompanied by an interesting "tabetic paralysis" of the lower extremities.

Of more especial interest is the case recorded by Allan Burns [4] in 1824. In his "Treatise on the Surgical Anatomy of the Head and Neck," he gives a detailed account of what is probably the first recorded case of chloroma. A young man—the age is not stated—had noted for some three months a fullness in the superciliary region of the brow. Later the vision in the left eye became affected, followed a fortnight afterwards by diplopia, exophthalmos and ocular pain. The swelling was incised but the pain persisted; the tumour increased in size and later sloughed. Other tumours developed—apparently arising from bone—and the right eye then began to bulge. Gradually the patient lost power in the legs as well as the capability of discharging his urine. Death concluded a state of extreme cachexia with decubitus. At the autopsy numerous greenish tumours were found in the lachrymal gland, the accessory nasal sinuses, the orbit, the surface of the skull bones and the dura; unfortunately the spine was not examined. Burns was, of course, unaware of the true nature of the disease, but gave an admirable discussion as to its probable type and also its relationship with fungus hæmatodes. "It presented none of the characters of that disease," Burns wrote: "the complaint seemed to me to have been one *sui generis* . . . how the disease was propagated, or what its nature was, are points on which we must confess our ignorance."

Another purely clinical case was recorded in 1917 by Schwab, Sale and Schmidt [35]. Their patient was a man aged 50, who experienced a sudden severe pain in the back. On the following day the legs were found to be weak, and in the course of the next three weeks they became totally paralysed and sphincter control was lost. Complete flaccid paraplegia was found on examination, with a sensory loss extending up to the fifth dorsal segment. A few days later signs of motor and sensory impairment appeared in the hands and arms, accompanied by difficulty in speech and swallowing. Enlargement of the liver and spleen was next demonstrated and hæmorrhages occurred in the skin. Blood examination revealed the leukæmic nature of the condition. The patient died sixty-four days after the onset of the symptoms. Post-mortem examination was not allowed.

In attempting to describe the various ways in which paraplegia may appear in association with leukæmia or chloroma, it will be advisable to adopt a classification based on pathology; to endeavour to deal with the problem according to the actual anatomical structures involved, and to specify the exact pathological variety of morbid process. For reasons already stated chloroma and the leukæmias will be treated together.

The paraplegic manifestations of these disorders will, therefore, be dealt with under the following seven heads:—

(1) Localized or diffuse leucocytic infiltration of the spinal cord.

(2) Localized or widespread softening of the spinal cord.

(3) Hæmorrhages into the spinal meninges.

(4) Infiltration of the spinal meninges by leucotic or chloromatous masses.

(5) Infiltration of the spinal nerve-roots.

(6) Infiltration of the peripheral nerves of the lower extremity.

(7) Manifestations of subacute combined degeneration of the spinal cord occurring in association with leukæmia.

(1) *Infiltration of the spinal cord* by aggregations of mature or immature leucocytes is not a common cause of paraplegia; it does not seem to occur in the chloromatous types. Such infiltration may be distributed diffusely throughout the substance of the cord or, on the other hand, may be collected into more localized leucoma nodules. The case recorded by Rosenstein [30] may be quoted in this connection.

Rosenstein (1881) described a case of leukæmia in a boy aged 7 who had been ill for some five weeks with enlarged glands and with general weakness. Examination of the nervous system revealed marked weakness of the legs with integrity of sensation. The knee-jerk was absent in one leg and barely obtainable in the other. The child was incontinent of urine. Post-mortem examination showed an infiltration in the lower dorsal and upper lumbar regions of the spinal cord with cells of the same type as were present in the visceral organs. The substantia centralis gelatinosa and the anterior and posterior commissures were the sites of maximum change. There was some dilatation of the central canal; the blood-vessels, including the finest terminal branches, were widely dilated, especially in the grey matter of the ventral horns. In general, the myelin and axis-cylinders were retained, although here and there they were lacking.

(2) Paraplegia may occur in the leucoses as the result of foci of *softening within the spinal parenchyma.* To this category belong the cases of Spitz [36] and of Baudouin and Parturier [2]. At various times such cases have been referred to as exhibiting areas of "myelitis"; detailed pathological studies make it clear, however, that the softened areas do not result from local inflammatory processes but are the secondary accompaniment of an affection of the spinal blood-vessels. Hypertrophy or hyaline degeneration of the vascular walls, particularly of the middle coat, predisposes to an accumulation of masses of leucocytes, and subsequent occlusion. In this way more or less extensive areas of myelomalacia are formed.

In 1901 Spitz referred to changes in the central nervous system in a fatal case of leukæmia. His patient had already been described clinically three years previously by Hirschlaff [14]. A woman aged 47 died from an acute leukæmia without showing any manifestations of neurological disease. At the post-mortem examination numerous focal lesions in association with the smallest blood-vessels were found. These were present in some degree in the white matter of the cervical region of the spinal cord, but were most plentiful in the pons. Each focus comprised an accumulation of round cells mostly mononuclear in type. Some of the larger lesions showed central necrosis, and resembled caseating tubercles.

Baudouin and Parturier's patient was a male aged 64, whose history was one of three months intense pain in the back, extending upwards to the epigastrium and downwards to the legs. This symptom was accompanied by weakness. Three days before admission to hospital the legs suddenly became quite flaccid and helpless. He was found to have a complete paraplegia with abolition of all reflexes and retention of urine. The patient died six days later. At the autopsy it was discovered that he had extensive leukæmic deposits throughout the viscera; a post-mortem blood-examination revealed a large excess of myelocytes. The condition in the spinal cord was one of "subacute diffuse myelitis," most marked in the upper thoracic regions but also present at the cervical and lumbar levels.

In some of the recorded cases localized softenings may be present in addition to a more diffuse infiltrative process throughout the cord. This is exemplified in the case recorded by Bloch and Hirschfeld [3]. Their patient, a child of 8 months, died from myelogenous leukæmia. Examination of the nervous system after death revealed a peculiar hardness in the consistency of the brain and spinal cord; this proved to be due to a diffuse cellular infiltration of both grey and white matter; in addition there was a generalized neuroglial proliferation. At the level of the third and fourth cervical segments a focal softening was visible.

(3) The evidence that *meningeal hæmorrhage* in the spinal region may cause neurological symptoms referable to the lower extremities is confined, so far as we can trace, to a single case. In a patient described by Olivier [26] there were no paralytic signs in the strict sense, though severe cramps in the legs had been present for some time. His patient was an alcoholic male of 61, whose symptoms were those of enlarged glands, purpura, fits and delirium. The post-mortem examination showed a leukæmic infiltration of the liver. The meninges of the brain and cord contained numerous areas of hæmorrhage; in the latter situation they were especially numerous, and were located chiefly over the ventral aspect of the first thoracic segment, the dorsal surface of the

third segment and on the fifth thoracic segment. There was no compression of the spinal cord, as in every case a considerable space intervened between the hæmorrhagic plaques and the cord.

(4) The commonest cause of paraplegia in leukæmia results from a more or less extensive *cellular infiltration of the spinal meninges.* This is particularly common in chloroma, a disease in which there is a special tendency towards the formation of cellular masses, particularly in relation to the dura mater. Cell masses of this kind were present in the following four personally observed cases, but the supposition that they may have caused paraplegia by pressure is not altogether supported by the microscopical examination of the spinal cord in two of the cases.

Case 1.—G. F. Q., a male, aged 19, was on October 24, 1928, transferred to Dr. Critchley's care at the National Hospital, Queen Square, by Dr. J. B. Rolleston with a diagnosis of leukæmic paraplegia. The history was of three months' general malaise, during this period he had been subject to headaches and appeared paler than usual. Three weeks ago he awoke with a sudden pain in the back which radiated forwards ; the legs were found to be numb and almost useless, and there was a difficulty in micturition amounting at times to an actual retention. Two weeks later his left eye became prominent, and two days afterwards he complained of some left-sided subcostal pain and vomiting. He was sent into the Western Hospital with the provisional diagnosis of typhoid. Here Dr. Rolleston found a condition of complete paraplegia. A blood-count showed 2,000,000 red cells and 136,000 white cells, of which a large proportion were myelocytes. The Widal reaction was negative.

Examination at the time of admission to the National Hospital revealed a very pale and emaciated man, completely paraplegic. Temperature 100·8° F, pulse 116, respirations 22. The mental state was normal. Both eyes were proptosed, especially the left ; ophthalmoscopic examination showed that the disc edges were blurred ; the blood-vessels were tortuous and engorged, and there were numerous hæmorrhages and areas of exudate. Lateral ocular movements were defective. No motor or sensory defect occurred in the upper extremities. Both legs were powerless except for very feeble attempts at flexion and extension at hip and knee joints The tone was flaccid and there was some diffuse muscular atrophy. The abdominal muscles and the lower eight intercostals were paralysed. No form of sensory stimulus could be felt over the legs or trunk up to the fifth thoracic segment. There was a feeble knee and adductor jerk obtainable on both sides ; otherwise all reflexes were in abeyance. There was lack of sphincter control with retention of urine.

The abdomen was distended and tympanitic : the liver was enlarged and the spleen was palpable a hand's breadth below the costal margin. Ecchymoses were present in the skin of the leg and thorax.

A blood-count gave the following result (Dr. Elizabeth O'Flynn):—

Red cells 1,270,000, Hb. 30, C.I. 1·2. White cells 229,000, polymorphs 50 per cent., myelocytes 41 per cent., hyaline 1 per cent., lymphocytes 5 per cent., transitional 2 per cent., eosinophils 1 per cent. Four megaloblasts were seen among 200 white cells.

Course.—The patient died on the fifth day after admission to hospital. During this period the temperature was constantly raised and varied from 99·6° to 103·8° F. He became weaker; delirium set in, and for the last twenty-four hours he was in a state of coma.

A post-mortem examination was carried out the next day by Dr. J. G. Greenfield.

Thorax.—The anterior surface of each rib was covered by a layer of green deposit which terminated abruptly at the costochondral junction. Similar material was found lying under the sternum and over the pericardium, where it seemed to have replaced the fatty remains of the thymus.

The *lungs* were somewhat nodular on palpation in their upper parts, but there was no evidence of tuberculosis nor any infiltration with chloromatous masses. A thin margin of collapse was found at the base of the right lung.

The *heart* was slightly enlarged. Some greenish streaks were seen under the epicardium along the line of the coronary arteries, and there were several cushion-like infiltrations on the right side of the interventricular septum. The right auricle and ventricle contained a very large greenish antemortem clot; the left ventricle a smaller one.

The *liver* was enlarged, weighing 2,680 grm. Numerous green infiltrations were seen on section along the lines of the portal vessels, and two large nodules of similar material were present on its anterior surface.

The *spleen* was large, congested and firm, weighing 250 grm.

The *kidneys* were swollen and pale, and the pelvis and perinephric fat of each was infiltrated with chloromatous material. The right kidney weighed 270 grm. In the left, which weighed 280 grm., an area of congestion and petechial hæmorrhages in the upper pole gave evidence of ascending pyelonephritis. The bladder wall was also inflamed. Infiltrations of chloromatous material were seen in relation to the lesser curvature of the stomach, and between the lobules of the pancreas.

Skull and brain.—Similar greyish-green deposits lay in the deeper layers of the scalp and in the dura mater covering the brain, and the folds of the falx cerebri and tentorium cerebelli were distended with similar greenish material. The lateral sinuses were filled with a pale clot. The infundibulum was also swollen and green and the basisphenoid in its upper part was replaced by chloromatous material which projected forward from it into the sphenoidal sinus as a cauliflower-like excrescence pushing the floor of the sella turcica upwards. Masses of greenish material were also found in the orbits lying on the orbital fat. These were more abundant in the left orbit than in the right.

The choroid plexus of the fourth ventricle was enlarged and bright green in colour.

Apart from the infiltration of the infundibulum, no green masses could be seen within the substance of the brain.

Spinal cord.—On removing the vertebral laminæ a deposit of grey green soft material was seen lying on the dura mater over the last cervical and the first seven thoracic segments and passing out a short distance through the intervertebral foramina. Similar deposits lay on the dura mater covering the anterior surface of the lumbar enlargement. On opening the dura mater the cord was seen to be slightly thinned and avascular at the level of the fourth, fifth and sixth thoracic segments.

Histologically the chloromatous masses and infiltrations all had an identical structure, being composed of masses of cells with rounded or lobed nuclei and a small amount of cytoplasm which stained fairly intensely with eosin. Some rather larger cells contained large, highly refractile granules which also tended to stain with eosin. A number of smaller cells indistinguishable from the eosinophil cells of the blood were also present. With benzidine staining, the cytoplasm of all the smaller cells showed oxydase granules and the granules of the larger cells also stained brown with this method. The latter granules also stained red with Scharlach R. in frozen sections and appeared to be a form of lipochrome. Apart from the numerous capillary vessels there was remarkably little stroma in the chloromatous masses, but fine reticular and collagenous threads could be seen passing through the tissue in all directions. (See fig. 1.)

The cord was examined at the level of every segment by a variety of staining methods. The most striking peculiarity was the presence in almost every vessel of a plug of leucocytes and myelocytes forming a fairly solid mass. Acute chromatolysis of some of the nerve-cells in the anterior horn was seen in the eighth cervical and first dorsal segments, and in the lumbar enlargement from the third lumbar to the first sacral segments. This appeared to be due to the passage of the emerging roots through the chloromatous masses in relation to the dura mater. At the level of the cord, which was observed to be thin and pale, viz., the fourth, fifth and sixth thoracic segments, a striking change was seen in the white matter, especially in the lateral columns. This consisted of areas of fenestration sometimes on the surface of the cord, but as often more deeply placed, and in some cases close to the grey matter. In these areas a large proportion of the nerve-fibres were swollen, their myelin sheaths either being broken up into fatty granules or stretched out into a thin peripheral ring. Within this ring two forms of body could be seen, one a nucleated cellular mass taking a faint blue stain in Scharlach R. sections and containing fine granules of degenerating myelin; the other a rounded homogeneous "cytoid" body, which on focusing proved to be a swollen axis cylinder. In longitudinal sections the fenestrated areas were seen to consist for the most part of rounded rather than elongated swellings of the myelin sheaths in which the myelin was broken down into granules, most of which did not stain very intensely with Scharlach R., but retained the double refractility of myelin and were, therefore, probably cholesterin compounds. In similar sections stained by Bielschowsky's method the axis cylinders, as they passed through these swollen areas, were seen to be swollen to more than twice their normal width. In some cases this swelling was oval or almost globular, in others more fusiform. Although these rarefied areas were usually situated in relation to one or two small blood-vessels, they were never concentric with the vessel, nor indeed were they of any fixed pattern. Those near the surface were more or less wedge-shaped with their bases outwards and consisted of a diffuse vacuolation affecting only a small proportion of the fibres. The most intense area was present in one lateral column in the fifth thoracic segment (fig. 5). This was an oval zone with its long axis radially placed, lying midway between the grey matter of the horns and the surface of the cord. In it almost every nerve-fibre was affected and the large vacuoles were only separated from one another by a very thin layer of tissue. Very numerous swollen axis cylinders were seen in this area, not only in the vacuoles but also in the tissues in the vicinity where there was no vacuolation. In the eighth and ninth thoracic segments similar areas were present, but in these the degree of fenestration and of swelling of the axis cylinders was less intense. These areas seemed to extend only for a comparatively short distance in a longitudinal direction, as the nerve-fibres in the next segments above and below them presented no evidence of disease. (See figs. 2, 3 and 4.)

Apart from these fenestrated areas the cord was comparatively normal. Early tract degeneration, in the form of swelling and partial disintegration of some of the myelin sheaths, was seen in the tracts of Goll, Flechsig and Gowers in the cervical segments and in the pyramidal tracts in the lumbar segments. In these tracts no swollen axis cylinders were visible and the swelling of the myelin sheaths was only of minor degree.

Case 2.—F. M., male, aged 8, was admitted to Charing Cross Hospital under the care of Dr. Gordon Holmes, on March 3, 1928, with the history of frequent spasms of severe abdominal pain of a fortnight's duration. Examination revealed a complete left-sided facial paralysis; the abdomen was somewhat full in the right iliac fossa but in other respects was normal. Temperature 98° F., pulse 120, respirations 24.

The abdominal pain persisted despite treatment. On the tenth day after admission he was found to have retention of urine, the bladder being distended to a point a quarter of an inch above the umbilicus; a catheter was passed and 17½ oz. urine withdrawn. The following day the bladder was again distended and a penile erection was noticed. When the child was told to stand it was found that he could not walk. Examination of the legs revealed a flaccid paraparesis with absence of the knee-jerks. The ankle-jerks were obtained and plantar stimulation gave a flexor response. There was no defect of sensation.

Next day the boy could no longer feel pin-prick over the legs or trunk up to the level of the eighth rib anteriorly. Lumbar puncture yielded a distinctly yellow fluid, containing a fine fibrin web. Total protein measured 1·3 per cent. with a marked excess of globulin. Cells numbered 2 per c.mm.

Within the course of the next few days the level of anæsthesia mounted as high as the sixth rib. A second lumbar puncture yielded a yellow fluid which clotted spontaneously in the test-tube.

A fortnight after the onset of paraplegia, nodules were felt in the groins. The child gradually grew paler and more listless, and developed several trophic sores. The degree of paraplegia became absolute with a total areflexia below the level of the lesion. The left-sided facial palsy was now much less noticeable.

A blood-count at this period revealed: Reds 3,150,000, Hb. 44, C.I. 0·7. Whites 15,700, polymorphs 54·3 per cent., large hyaline 0·3 per cent., small lymphocytes 22·3 per cent., myelocytes 20 per cent., myeloblasts 3 per cent. Some degree of poikilocytosis and anisocytosis.

The nodules in the abdomen became gradually larger but the spleen was not palpable until six weeks after the onset of paraplegia. A week later three nodules were felt on the scalp. The child now became still drowsier and lost weight. Purpuric patches appeared in the skin. Pains were complained of in the head, chest and ears. The general condition deteriorated markedly and there were bouts of generalized tremor. The child died on May 22, 1928, eighty days after admission to hospital.

Throughout the course of the illness the temperature had been raised, at times reaching as high as 104° F.

Autopsy was performed the next day by Dr. Gordon Holmes.

Thorax.—Flat masses of deposit lay on the outer aspects of the ribs and posterior surface of the sternum. A large mass was present on the right side of the vertebral column projecting into the pleural cavity. Soft glands were seen at the roots of the lungs, and section of both organs showed infiltration. The heart was normal except for a gland on the anterior aspect of the pericardium.

Abdomen.—There was a chain of retroperitoneal glands in the abdomen.

Spleen.—Enlarged, weight 200 grm.

Liver.—Weight 810 grm.

Kidneys contained numerous small areas of growth, chiefly in the cortex. Two glands were found in association with the wall of the bladder.

Skull.—Several flat, soft, greenish nodules lay beneath the aponeurosis of the scalp. When the brain had been removed, other similar tumour masses were found. The meninges were infiltrated in various places, notably at the anterior end of the falx and in the dura covering the temporal bones, the basi-occipital and the lateral sinus. Masses of growth lay underneath both petrous bones.

Spinal canal.—Large greenish masses were seen in the epidural space ringing the cord at the level of the eighth cervical and the first thoracic segments. Flatter, more sessile masses were also found lying on the dura mater which covered the lower six thoracic segments. (See fig. 5.)

On cutting through the dura mater the cord was found to be pale, but otherwise normal down to the eighth thoracic segment, but from this level downwards it was shrunken and brownish, and adherent to the dura mater. From the ninth to the twelfth thoracic segments the central part of the cord was quite diffluent. In the lumbar segments it was less softened, although here also no trace of the normal structure of the cord could be seen.

As it was considered advisable to retain the cord as a museum specimen thin transverse slices were taken only from the first thoracic and the ninth thoracic segments. These were embedded in celloidin and stained by Nissl's method (toluidin blue), hæmatoxylin and van Gieson, Mallory's aniline blue—Orange G. and Loyez myelin sheath stain.

Sections from the first thoracic segment showed little abnormality except a fairly severe degree of chromatolysis in some motor cells of the antero-lateral and postero-lateral groups, and degeneration in the columns of Goll and Flechsig. In these tracts there was some degree of vacuolation of the cord caused, apparently, by swelling of the myelin sheaths and disintegration of the myelin similar to that seen in the cervical segments in Case 1. It seemed to correspond to an early stage of ascending tract degeneration.

At the level of the ninth thoracic segment there was complete disintegration of the nervous tissue of the cord. The meninges were considerably thickened. The outer layers of the arachnoid were infiltrated with polymorphonuclears and larger cells with lobed or rounded nuclei similar to those seen in the chloroma masses in Case 1. Similar cells were also seen in the septa of the anterior roots, in which also many of the nerve-fibres were considerably swollen.

In the cord it was only possible to distinguish any of the original structure by the greater vascularity and the larger number of nuclei in the region of the grey matter. The capillary vessels here seemed to be considerably more numerous than normal and were linked to one another by thin collagen strands. Otherwise the tissue consisted almost exclusively of masses of fat granule cells, among which were a few small rounded nuclei with an unrecognizable cell body. In one anterior horn were the degenerated remains of three or four nerve-cells. These consisted chiefly of lipochrome granules with the remains of the nucleus, as the cytoplasm had been almost entirely absorbed by mononuclear phagocytes. Fat granule cells were also found in large numbers infiltrating and distending the meshwork of the pia mater in the antero-mesial fissure and around the margin of the cord. (See figs. 6 and 7.)

Case 3.—J. W., male, aged 15, was admitted to Charing Cross Hospital on November 6, 1922, under the care of Dr. Gordon Holmes. Five days previously his legs had suddenly become weak and felt numb. There was at the same time some hesitancy in commencing micturition.

On examination he was found to be well nourished but pale. There was a flaccid paralysis of both legs with impairment of sensation up to the level of the second lumbar segment. The knee and ankle jerks were exaggerated; both plantar responses were extensor in type. There was an absence of sweating below the waist-line. There was no loss of sphincter control.

In the course of the following month the legs became still weaker; he developed incontinence of urine with retention. The right arm was also found to be weak and the biceps-jerk on that side was unobtainable. Small glands were felt in the axilla and the groin.

Two weeks later the weakness in the arm had disappeared. The legs were now becoming spastic and involuntary flexor spasms occurred. The patient began to complain of pains radiating round the waist and down the right thigh. The lymphatic glands were now definitely enlarged and the spleen was palpable. A blood-count at this stage showed: reds 3,800,000, hb. 62, C.I. 0·8. Whites 16,000, polymorphs 20 per cent., lymphocytes 55 per cent., lymphocytes (large) 17 per cent. A few myeloblasts, myelocytes, and normoblasts were seen. There was polychromophilia and slight poikilocytosis.

Ten weeks after admission to hospital he developed a paralysis of the left side of the face and of the palate; he became deaf in the left ear. The paraplegia was now more profound and the upper level of analgesia had extended as high as the seventh thoracic segment.

Three months after admission nasal and conjunctival hæmorrhages appeared.

Three and a half months from the time of entry into hospital a condition of leukæmic retinitis first made its appearance; the discs were swollen, the veins engorged, hæmorrhages and white patches of exudate were visible in the retina.

Following treatment by X-rays some degree of improvement in the legs resulted and also in the sphincter control. The retinitis advanced, however, and the patient's general condition deteriorated. He developed deafness and a profound visual defect; purpuric areas appeared over the legs. Death occurred four months after admission.

At the autopsy typical leukæmic changes were demonstrated in the viscera. No morbid change was demonstrable in the brain. The spinal cord and its membranes, however, were the seat of various pathological processes:—

(1) A few small hæmorrhages were visible in the pia-arachnoid.

(2) Two large epidural leucoma-masses were present at the second and seventh thoracic levels respectively.

(3) The underlying cord showed only slight changes of compression, being somewhat œdematous and containing a few hæmorrhages.

(4) The spinal roots were in many places infiltrated by leucoma-masses.

Case 4.—J. P., male, aged 11, was admitted to the Queen's Hospital Birmingham, under the care of Dr. Mackey, on April 5, 1926. Symptoms began with a seven weeks' history of pain in the dorso-lumbar region, particularly on the left side. He became weak and lost flesh; three weeks before admission his legs became weak, preventing him from walking. At the same there was a little difficulty in commencing micturition. The legs grew weaker until a state of complete paraplegia supervened five weeks after the onset of symptoms.

Examination revealed a pale wasted boy with proptosis of the left eye. The right side of the face was swollen and the veins over the right side of the forehead were more dilated.

The abdomen was protuberant, and the superficial veins were dilated. The liver was enlarged to the extent of three fingers' breadth below the costal margin. A large mass was palpable in the lumbar region, irregular in outline, extending from the costal arch above down to the iliac crests. The spleen could not be felt.

The motor and sensory systems were normal over the arms and upper part

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of the trunk. The lower extremities were completely flaccid and powerless. Postural and vibratory sense were lost in the legs but tactile and painful stimuli were correctly appreciated. Knee and ankle jerks were absent; there was a bilateral Babinski response.

Cerebrospinal fluid examination gave the following report. Straw-coloured fluid, no cells. Marked excess of albumin and of globulin. Sugar 19 mg., chlorides 0·8 grm. per cent.

Skiagraphy revealed: (1) a mediastinal tumour and (2) an erosion of the anterior surface of the second lumbar vertebræ.

The clinical diagnosis was made of a bilateral suprarenal tumour with metastases in the mediastinum and spinal canal.

Whilst in hospital the patient became more cachectic and drowsy; there were frequent slight epistaxes. Pains in the legs were constantly complained of, and vomiting was an occasional symptom. He finally became comatose and died two and a half months after the first symptom.

The autopsy was performed the following day by Dr. O. Brenner.

Spine and spinal canal.—In the dorso-lumbar regions there was a soft, red mass resembling partially organized blood-clot, wrapped closely around the spinal cord. The cord itself appeared normal except for a small red spot in the right anterior horn in the lumbar region. The consistency of the second lumbar vertebræ appeared softer than usual.

The changes in the visceral organs were characteristic of leukæmia. The thymus was greatly enlarged with areas of focal necrosis visible on cross-section. The spleen was shrunken and atrophic; weight, 50 grm.

Both kidneys were uniformly much enlarged (weight: right 540 grm., left 530 grm.).

Some of the lumbar and many of the mesenteric lymph glands were enlarged.

Longitudinal section of the femur showed that it was filled for about two-thirds of its length with a greyish-red gelatinous marrow.

Histological examination (Professor Haswell Wilson) of the spinal cord revealed a leukæmic infiltration of the meninges and of the sheaths and interstitial connective tissue of the anterior and posterior nerve-roots. The process spread into the cord via the anterior fissure and the sheaths of the blood-vessels. The nerve-cells, with one or two exceptions, were normal. Microscopic examination of the viscera showed a generalized leucocytic infiltration.

There are a number of cases on record similar in essentials to these four cases described. The majority had the characteristics of chloroma, although pure leukæmia has been diagnosed in some.

Eichhorst's case [7] illustrates such focal aggregation of leucocytic material outside the spinal cord. His patient, a young man of 17, was admitted to hospital for enlargement of the glands and general weakness. While an in-patient he developed in the course of a week a spastic paraplegia, with sensory loss and bladder trouble. The blood examination gave the picture of a myeloid leukæmia. At autopsy it was found that the fifth, sixth and seventh segments of thoracic cord were compressed by a greyish tumour-mass of glandular appearance about 3 cm. long lying along the posterior aspect, especially on the left side. The cord at that point was severely compressed and softened, and secondary degeneration could be traced above and below the site of the mass.

Harris and Moore in 1902 [10] demonstrated before the Manchester Pathological Society the spinal cord of a case of chloroma occurring in a boy of 14. The first symptom was severe pain of sciatic distribution persisting up to the time of death. Two weeks before the end he became partially paralysed in arms and legs. At the post-mortem examination a nodular mass was found on the inner aspect of the dura and the periosteum of the vertebræ.

In the same year, Rosenblath [29] described a case of chloroma in a boy of 15, who complained of pain in the sciatic region when the leg was extended; although the knee-jerks became sluggish no actual paralysis supervened. The patient died, and the pathological aspect was studied by Rosenblath and also independently by Risel [27]. A mass of chloromatous material lay between the bone on the inner aspect of the lumbar spine and the dura mater; a similar mass measuring 10 cm. by 1 cm. was present in the lower thoracic region. The posterior roots in the lumbar segment as well as the sacral plexus were implicated in the masses. Histological examination of the cord revealed a degeneration in the posterior columns above the area of root damage.

A case of chloroma in a male of 19 was recorded in the following year by Gumbel [9]. This patient developed four weeks before death the signs "of a beginning myelitis." Pathological examination showed an infiltration of the epidural fat with green tumour-masses, involving especially the nerves of the lower sacral region. The anterior and posterior roots of the lumbar segments were thickened in sausage-like manner. The spinal cord was constricted at the cervico-dorsal junction, and in the dorso-lumbar region the cord was softened.

Weinberger (1907) [40] reported the case of a lad of 15 who complained of stiffness of the spine for one month before admission. Pains later appeared in the left thigh, and there was some difficulty in micturition. Whilst in hospital he developed weakness in the arms and legs, with dysæsthesiæ and defective sensibility. The tendon-jerks were increased, there was ankle clonus and bilateral Babinski responses. He became doubly incontinent. After death infiltrating thickenings of chloromatous material were found in connection with the periosteum and dura of the posterior part of the spine, especially in the thoracic region. The cord itself was severely compressed.

In 1909 Saltykow [32] described a female patient of 37 who showed, two months before death, a tumour in the left side of the neck and a weakness of the left arm. She was regarded as a case of tuberculous spondylitis, but at the autopsy a mass of chloromatous matter 1 cm. thick was found lying between the bodies of the vertebræ and the spinal dura. It extended longitudinally from the fifth to the tenth thoracic segments. The cord was compressed and softened.

Stursberg's case (1914) [38] was that of a man of 30 suffering from myelogeneous leukæmia who experienced a sudden pain in the back and legs. The following day both legs were completely paralysed and pain persisted in the legs. A condition of flaccid paraplegia with analgesia remained up to the time of death twelve days later. Pathological examination demonstrated a myeloid mass in the spinal dura compressing the cord, particularly in the lower dorsal and lumbar regions.

Sauer [33], in the same year, reported a case of chloroma in a man of 36. His symptoms were those of severe pain in the right leg with some defect of power, especially in dorsiflexion of the foot. There was tenderness on deep palpation over the course of the right sciatic nerve, and Lasègue's sign was positive on that side. Pain and thermal sensibility was diminished over the distribution of the third, fourth and fifth lumbar and the sacral segments. At the post-mortem examination it was seen that the whole of the anterior aspect of the spinal dura was covered with a layer of chloroma-material which became thicker towards the lower end.

Miermet's patient [21]—recorded in 1914—was a boy of 15, whose illness started with a sudden giving way of the leg. During the next four months the same symptom recurred four times, and at the end of that time he was admitted to hospital because he could not walk nor void his urine. A lumbar puncture gave a yellow fluid containing an excess of cells and of protein. The diagnosis of spinal tumour was made and a laminectomy performed. At operation the cord was found to be surrounded by "granulation tissue," and the case was then regarded as one of tubercle. An emulsion of the granulomatous tissue was, however, not lethal when injected into a guinea-pig. Later, a swelling developed at the site of the scar, and was thought to be a cold abscess. Then numerous blue-black lumps appeared, and the diagnosis was changed to that of myeloid sarcoma. The case ultimately proved to be one of chloroma, however, and lumps of greenish-grey tissue were found in the spinal meninges.

Bassoe reported in 1918 a case of spleno-medullary leukæmia in a woman aged 28. Three years after the onset of her anæmic symptoms she developed a sudden chill; the day after, the legs were numb and so weak that she could not stand. She was completely paraplegic in the course of one day and two days later she became febrile. Difficulty in urination appeared next, amounting later to a complete retention. She showed an absolute paraplegia with loss of sensation up to the fifth rib; the tendon-jerks were absent except the left ankle-jerk, and plantar stimulation gave extensor responses on both sides. There was pain on pressure over the fourth, fifth and sixth thoracic spines. The patient was persistently febrile and developed bedsores; she died five weeks after the onset of paraplegia. In addition to the typical visceral manifestations of leukæmia, there was found at autopsy a thickening of the dura in the fourth, fifth and sixth thoracic regions which was firmly adherent to the bodies of the vertebræ. The cord was surrounded by thickened and infiltrated membranes causing partial necrosis of the spinal parenchyma, especially in the posterior aspect in the fifth thoracic segment.

In the following year a further case of chloroma with deposits in the spinal meninges of the mid-thoracic region was reported by Lewis [18]; unfortunately there are no clinical details as to the neurological manifestations in the legs.

Heissen's valuable paper appeared in 1925, and in it he quoted a case of chloroma occurring in a woman of 34. For five weeks she complained of backache and for two weeks of cramps and stiffness in the legs. The day after the first appearance of this latter symptom, dysæsthesiæ were noted in the left leg At the same time she suddenly lost power and sensation in the lower extremities and became incontinent. On examination a state of flaccid paraplegia was encountered with sensory loss up to the nipples. The reflexes were unobtainable; bladder and rectum were paralysed. The cerebrospinal fluid was cloudy and escaped slowly from the needle; the pressure measured only 70. There were 375 cells per c.mm. including polymorphonuclears and immature myelocytes. The total protein was markedly increased. Death occurred seventeen days later. At autopsy a layer of green chloromatous deposit was found outside the dura of the second to fifth segments of the thoracic spine. The cord in this area was compressed and on trans-section showed softenings and hæmorrhages.

In the same year, Sturrock and Jeffery [37] demonstrated at the pathological meeting of the Neurological Section of the Royal Society of Medicine a specimen of chloroma in the vertebral canal causing paraplegia. The patient was a boy of 14, in whom paralytic signs had developed four weeks before death. Fuller clinical details are unfortunately not given.

(5) Symptoms of a paraplegic order may also occur in chloroma from *infiltration of the spinal roots of the lumbar and sacral plexuses* without any actual compression of the cord. An example of this type is illustrated by the case recorded by Klein and Steinhaus (1904), [17]; their patient, a man of 38, had complained for six weeks of pain in the right leg and examination yielded signs regarded as evidence of neuritis of the right sciatic nerve. Autopsy revealed numerous chloromatous nodules along the vertebral column, not compressing the cord, but surrounding the roots.

(6) Another rare cause of paralytic manifestations in association with the leukæmias is to be found in the occurrence of changes *in the peripheral nerves*. Instances of "leukæmic polyneuritis" were referred to by Müller in his Inaugural Address of 1895 [24]. A particularly striking example was published by Wilfred Harris (1921) [11] and [12]: A youth of 17, complained first of weakness of the legs; five weeks previously the legs had become stiff and a fortnight later he became unsteady on his feet and noticed numbness and tingling of the fingers. The gait was feeble and uncertain, there was weakness of dorsiflexion of the feet with partial reaction of degeneration in the leg muscles. Tactile and pain sensibility were diminished up to the knees. Patellar, Achilles and fore-arm jerks were absent and no plantar response was obtainable; the cremasteric reflexes were normal. There was no sphincter disturbance. The patient died about twelve weeks after the onset of symptoms. Post-mortem revealed the typical changes of leukæmia with leucocytic infiltration of the peripheral nerves. Harris did not regard the paretic manifestations as the result of the infiltration of the nerves, but rather as an expression of a polyneuritis due to an obscure toxin.

Infiltration of the peripheral nerves in leukæmia was also mentioned by Ball, in the discussion following Holmes's paper at the Association of Physicians.

(7) The last anatomo-pathological process which may be responsible for the presence of spinal symptoms in the leukæmias is seen in those very rare cases of *combined degeneration of the cord*. Although the

great majority of instances of funicular myelitis or subacute combined degeneration of the cord are clinically associated with a morbid blood-picture which approximates to the "pernicious" anæmia type, nevertheless departures from this type are common. Thus, one may meet with cases of severe spinal signs accompanied by a normal blood-count. Moreover, the characteristic clinical or pathological manifestations may—very infrequently—be associated with other hæmatological disorders, such as Hodgkin's disease (McAlpine [20]), streptococcal anæmia (Lorimer [19]), chronic icterus (Minnich [22]), and Addison's disease (V. Kahlden [16]), as well as sprue and malaria. According to Collier [5] they may also occur in the leukæmias, but detailed clinical and pathological reports of typical cases of this association are wanting although there are some suggestive records in the literature [32].

In the original monograph of Minnich (1892) on spinal disease in pernicious anæmia, there are a few brief references to the occurrence of similar pathological changes in a case of leukæmia, and Minnich reproduces illustrations of the spinal cord which show degeneration in the posterior columns. We are told that this case was without neurological signs or symptoms during life.

Two years later appeared Müller's thesis in which he described the spinal cord changes in a case of splenic leukæmia. Unfortunately no clinical data are available. He found a slight sclerosis in the columns of Goll and partly also in those of Burdach, with loss of nerve-fibres and increase of neuroglia. This process was most intense in the cervical region. The ground bundles contained some degenerated fibres and lacunæ. There were no changes in the grey matter or in the anterior or lateral zones of the white substance. The blood-vessels and the anterior and posterior roots were normal.

Nonne [25] in 1897 reported clinical and anatomical details of two fatal cases of leukæmia, in neither of which had there been any neurological signs during life. In the first case (that of a man aged 59) there were numerous small foci of change in the myelin, especially in the cervical cord. The axis-cylinders were swollen in these areas and in the intervening substance the neuroglia had proliferated. These foci were so minute as to elude perfunctory search; they were asymmetrical in distribution and lay chiefly in the anterior pyramidal tracts, the lateral columns and the posterior columns, in this order. There was no anatomical association between the foci and the blood-vessels. In addition to these changes, there was a slight sclerosis of Goll's columns in the cervical region, and also to a less extent in the upper and mid-thoracic portions. Nonne's second case (a man aged 31) was also characterized pathologically by focal changes in the white matter, especially in the anterior columns. No sclerosis of Goll's or Burdach's columns was seen in this case.

Gordinier and Lartigau in 1902-3 [8] described a case of lymphatic leukæmia in which a sclerosis of the posterior columns was demonstrable in the upper thoracic region of the cord after death. We have been unable to secure clinical and histological details of this case.

The only instance of this kind associated with chloroma is of doubtful authenticity. Dock and Warthin in 1904 [6] reported a fatal case of chloroma in a man aged 45. No objective or subjective signs were present referable to the central nervous system. At the autopsy the spinal cord appeared normal, but histological evidence of "atrophy and degeneration" was present.

Pathological Discussion.

Throughout this paper no separation has been made between neurological syndromes complicating the leukæmias and those occurring in association with chloroma. This arrangement has been followed in accordance with the modern conception of leukæmia and chloroma as being of essentially similar nature. The latter clinical state is differentiated primarily by a greater tendency towards the formation of "heterotopies," or leucocytic infiltration *en masse*: secondly, by the presence of a characteristic green tint to the cell-masses; and thirdly, by an acute course. Heterotopies may, however, occur in other varieties of leukæmia, as evidenced by the so-called "leucosarcomatosis" of Stursberg, and the cases spoken of as chlorosarcoma. Typical green coloration may also be seen in the other types of leukæmia. We are justified, therefore, in treating chloroma and all other forms of leukæmia as varieties of a wider group of hæmoblastosis, in the sense of Orth.

Although the number of instances of spinal involvement in the course of leukæmia is not sufficiently great to warrant dogmatic conclusions, it appears that certain varieties of pathological change are more prone to occur in particular hæmatological types.

In some cases there may be a diffuse permeation of the grey and white matter of the cord with cell-elements which do not form dense heterotopies. A reactionary gliosis may follow so as to produce a diffuse sclerosis of the cord. This variety of pathological change seems confined to the leucoses proper. At times the cell-elements may become aggregated here and there to form focal leucoma nodules which—unlike the heterotopies—are situated strictly within the spinal medulla.

The commonest cause of spinal symptoms in the leukæmias is obviously an infiltration of the spinal meninges with leucocytic masses. This process is more frequent in association with the clinical picture of chloroma. Thus out of a total of seventeen cases twelve were developed in connection with chloroma and five with leukæmia. The neoplastic cell-masses usually lie between the inner aspect of the vertebræ and the spinal cord. They are more or less firmly adherent, either to the periosteum of the vertebræ or to the dura mater. In any case the epidural fat becomes infiltrated and ultimately replaced by the heterotopy. The infiltrating mass may lie anteriorly or posteriorly, or may totally encircle the cord. As a rule the mass is of some length and may extend from one end of the cord to the other. The infiltrations are smooth in appearance and vary in tint from white or pale yellow to a distinct green; they are india-rubber like in consistency; German writers often describe them as resembling the rind of bacon (Schwarte). It may be possible by exercising care to dissect the masses off the periosteum or dura mater.

Frequently the infiltration spreads so as to involve the anterior and posterior nerve-roots; rarely, the roots alone are implicated. Sometimes the infiltrating tissue follows the course of the roots and insinuates itself into the paraspinal fascia and muscles via the intervertebral foramina. At times the opposite process is demonstrable; that is, the heterotopy may take origin in the tissues lying alongside the bony column, and following the posterior primary divisions of the dorsal nerves, enter the spinal canal by way of the intervertebral foramina.

The secondary changes in the spinal cord vary from one case to another. In some cases at the level of the largest cellular masses the cord appears constricted and pale, and cross-section shows an anæmic cord in which the grey matter can scarcely be distinguished from the white columns. The pia mater over this region shares in the ischæmic process by loss of the fine vascular ramifications. In other cases the cord is obviously hyperæmic at the site of the tumour; it is swollen and injected and on cross-section pin-point hæmorrhages may be seen in it. This appearance, which is reminiscent of that of acute myelitis, is distinguished from it by the absence of cellular exudate, and is probably the result of acute infarction. In fact it appears probable that both the anæmic and the congested appearances may be caused rather by the obstruction of blood-vessels than by the actual compression of the spinal cord by the cellular masses.

Compression of the cord may undoubtedly also play a large part in the pathogenesis of the condition, as is shown by the slowly progressive history in some cases, but in others the fulminating onset of the paraplegia is more suggestive of a thrombotic softening of the cord.

The condition of the spinal cord in our second case indicates how severe and extensive this condition of ischæmia may be. In it the lower part of the cord from the ninth thoracic segment downwards was completely disorganized with the disappearance of all the nervous structures, and persistence only of the walls of the blood-vessels, the membranes and the connective tissue septa. Such a condition must be caused by a widespread deprivation of blood supply, and can be paralleled in our experience only by cases in which many of the intervertebral arteries have been obstructed or compressed by tumours or bony overgrowth. In the cases under discussion it is easy to see how such a vascular obstruction might occur. It has been noted that the cellular masses frequently pass out through the intervertebral foramina compressing the nerve-roots, and in doing so are likely to compress also the segmental arteries and veins. Thrombosis of vessels may also be caused by the degenerative changes in the walls of the vessel or by the leucocytic clots inside them which have been seen in some cases. But these appearances may be secondary to the ischæmia rather than the direct cause of thrombosis. In any case it seems probable that the severer degrees of myelomalacia which have been described in association with the meningeal infiltrations of chloroma and leukæmia should be attributed rather to ischæmia than to direct pressure.

It is, however, more difficult to decide the pathogenesis of the small areas of softening or fenestration which Nonne described in his two cases and which were present in our first case. That the condition was the same in Nonne's cases and our own is clearly demonstrated by the beautiful drawings illustrating Nonne's paper which might equally have been drawn from sections of our case.

This pathological condition resembles in many details that seen in subacute combined degeneration of the cord, but differs from it not only in its patchy distribution, but also in the great swelling of the axis-cylinders associated with it. Nonne accepts the swelling of axis-cylinders as being an early stage in the process of fenestration, and this view is supported in our opinion by the presence of swollen axons round the periphery of the fenestrated areas. It is possible that Schultze's case (1884) [34] represents a similar early stage spread over a wide area. No clinical details of this case are available beyond the bare statement that the patient was suffering from leukæmia. On examination of the spinal cord he found a diffuse swelling of the axis-cylinders throughout the spinal cord. This was most evident in the cervical enlargement and in the lateral (and to a minor degree the posterior) columns. There was no trace of inflammatory cells. Schultze regarded the pathological condition as a disorder of the nutrition of the axis-cylinders as a result of the abnormal blood condition and compares it with a similar swelling of the axons of the spinal cord which he had found in cases of nephritis.

Similar swelling of axons has been described by Gordon Holmes [15], and by Roussy and Lhermitte [31] in concussion of the spinal cord by wounds. The latter authors call the condition "acute primary degeneration of myelinated fibres," and point out that the swellings on the axis-cylinders are always terminal and indicate fragmentation or rupture of the axons. That this condition may be due to a variety of causes which diminish the vitality of the neurons in the cord is indicated by its occurrence in such diverse conditions as injury of the cord and leukæmia. In the latter case it probably indicates a local necrosis of the more specialized nervous elements resulting from ischæmia of rapid onset. This theory of origin does not at first sight agree with Nonne's observation that the areas of fenestration do not appear to have any relation to blood-vessels. In our case a few small vessels were usually seen either in or close to them, but since the spinal vessels are more or less radially arranged it would be necessary to examine several transverse sections in order to prove this point with certainty. The fact that several of the most severely fenestrated areas were found somewhat deeply placed in the white matter, both in Nonne's cases and our own, may be taken as evidence against the view that they were caused directly by the pressure of a tumour or cell-mass, and indeed they are rarely seen in cases of spinal tumour. It seems, therefore, most probable that they form merely a variant or an early and partial form of the larger areas of myelomalacia which have been so commonly found in leukæmic cases. If this view be taken, it becomes impossible to ally the condition to the somewhat similar appearances seen in subacute combined degeneration. This is in accordance with the views of Weil and Davison [39], who in a wide survey of the literature could find no evidence that this form of spinal disease may be associated with leukæmia. It is true that in eighteen of their twenty-two cases of leukæmia and chloroma they accepted the clinical absence of paraplegic symptoms as evidence that no spinal disease existed, and did not confirm this pathologically. But if the fenestrated areas found by Nonne and ourselves were indeed an early state of subacute combined degeneration of the cord, we should have expected that more typical and complete cases of the latter disease would have been found in association with leukæmia. That no such case has hitherto been published may, therefore, be taken as evidence against the relationship of the two pathological conditions.

It appears, therefore, that the most common factor in the production of paraplegia in cases of leukæmia or chloroma is anæmia or ischæmia of the spinal cord. The partial anoxæmia of the tissues which is inseparable from a severe anæmia must in many cases contribute to the effect produced by compression or thrombosis of the spinal arteries, but it is unlikely that any degree of anæmia which is compatible with life can, of itself, so lower the nutrition of the nervous tissue as to lead to its disintegration.

Clinical Discussion.

In the diagnosis of leukæmic paraplegia it is necessary to obtain accurate neurological observations on the degree of weakness, the extent of sensory loss, the state of the reflexes and the integrity of the sphincters. The importance of these points lies in the fact that in states of severe constitutional disorder such as occur in the hæmatopoietic diseases, a condition of "pseudo-paralysis" is apt to appear. This holds true, especially in the case of children, in whom weakness of the trunk and limb musculature or tenderness of the tissues may produce an akinesia algera which may closely simulate a paraplegia of spinal or peripheral origin. A highly instructive example in point is illustrated in the case recorded by Rolleston and Frankau [28]. Their patient, a boy of 5, had complained for five days of pain in the abdomen and difficulty in walking. When examined he was found to be unable to sit up, and there was tenderness over the lower dorsal and upper lumbar vertebræ. The paraspinal muscles were distinctly rigid. The case strongly suggested one of caries of the spine, but the subsequent appearance of enlargement of the liver, and of nasal, renal and retinal hæmorrhages, pointed to a leukæmia. A blood-count confirmed this diagnosis. At the autopsy typical leukæmia changes were found; the vertebræ were softened, but no actual lesion lay in the cord or its membranes and no spinal compression had occurred. In this case, therefore, the changes in the vertebræ set up pain and stiffness in the surrounding muscles, which accounted for the difficulty in sitting up and the pseudo-paraplegic symptoms.

When dealing with the symptomatology of the true paraplegic manifestations of the leukæmias it will be well to consider first those cases with the pathological picture of masses infiltrating the epidural tissues as representing the commonest variety. Of the seventeen cases, including the four personal examples, fourteen were in males and three in females. The age at which symptoms appeared varied from 8 to 38 years, with an average of 20·6 years.

The early symptoms in the majority of cases were some subjective sensory complaint, usually pain. This is usually severe and is frequently of sudden onset. It is commonly referred to the back, but it may also affect one or both legs. In several instances this has led to the diagnosis of sciatica. Occasionally (as in Cases 1 and 2) the pain may be referred to the abdomen, suggesting—as in the former instance—the diagnosis of typhoid. Pain is not only the first symptom to appear in the majority of cases, but it is usually the most persistent feature. Sometimes the earliest symptom is a feeling of stiffness of the legs or of the muscles of the back. A sensation of numbness, deadness, or pins and needles is scarcely ever the initial symptom.

A short time after the onset of pain other clinical features appear. This interval is variable; in some cases it may be as short as a day, rarely is it longer than six weeks. At the end of this time the patient experiences, usually with some abruptness, dysæsthesiæ in the legs, accompanied or followed very shortly by weakness in the lower extremities. This latter symptom may be fulminating in appearance, being sudden in onset and immediately attaining its maximum intensity. At other times the paraplegia develops more gradually, so that a week or more elapses before the paralysis is complete. Once fully developed no improvement is to be anticipated as a rule, although in Case 2 some relief followed X-ray therapy. Objective sensory changes accompany the paraplegia and may be absolute in degree. Usually the subjective sensory disorders antedate by a short interval the appearance of objective change.

Bladder disturbances accompany the paraplegia and lead in the more severe cases to retention of urine and fæces. Sometimes, as in Case 2, difficulty in micturition may precede manifestations of paraplegia. Priapism is a characteristic, though rare, manifestation in leukæmia, and in the spinal cases may be the expression either of the paraplegia or of an actual leucocytic infiltration of the corpus cavernosum.

Bed-sores develop with marked rapidity once the paraplegia is established. In those instances in which laminectomy has been performed the operation scar may break down. Constitutional symptoms appear either before or after the onset of paraplegia. The patient rapidly loses weight and becomes febrile. Visceral manifestations of leukæmia may develop at this stage and betray the true nature of the case, but it is important to note that frequently there are no somatic indications of chloroma or leukæmia until long after the development of spinal symptoms.

The physical signs in the cases of leukæmic paraplegia present nothing characteristic. It is perhaps striking how profound the degree of paraplegia may be; often the lower extremities are completely powerless and atonic, with tendon-jerks and plantar responses unobtainable. Percussion of the spine not infrequently reveals tenderness over certain of the spinous processes and rigidity of the para-spinal muscles is common.

A step-like ascent of the level of the paraplegia has been noted in certain cases. The level of the spinal lesion may at first lie in the mid-dorsal region, but, after an interval, signs may appear in the arms. Such a progression suggests either an upward spread of the epidural masses, or, alternatively, the development of focal softenings at a higher level of the cord.

Examination of the cerebrospinal fluid has been carried out in but few cases. In cases with complete spinal block the typical "loculation syndrome" is, of course, to be expected. The important diagnostic point in these cases, however, lies in the possibility of demonstrating in the fluid immature white cells such as myelocytes or myeloblasts (cf. Heissen's case). The presence of such cells would, of course, be diagnostic of myelogenous leukæmic paraplegia, but their absence in no way precludes the diagnosis.

In reviewing the case-reports contained in the literature, it is striking how often the true nature of the disease has escaped recognition until demonstrated at autopsy. The obvious reasons for this lie firstly in the intrinsic rarity of the leukæmic types of paraplegia, but the second and more particular cause depends upon the fact that the manifestations of disease of the hæmatopoietic system may be so slight as to be overlooked. It appears, therefore, that the occurrence of a sudden paraplegia, preceded for a time by severe pain in back or legs, and followed by fever, pallor and loss of weight should, when occurring in a young adult, suggest the possibility of a leukæmic or chloromatous origin. When such a neurological picture presents itself, it will be necessary by examination of the blood and blood-forming organs, to exclude this diagnosis.

The presence of local muscle atrophy in the legs with reaction of degeneration suggests an implication either of the spinal roots or of the peripheral nerves. This process may occur as an isolated neurological state, in which case there will be an absence of the tendon responses and a peripherally distributed type of sensory impairment. On the other hand, the signs of lower motor neuron disease may be masked by coexistent paraplegic manifestations.

A point of great interest lies in the problem whether subacute combined degeneration of the cord may occur in cases of leukæmia. In most of the recorded cases in which a pathological appearance somewhat similar to that of this disease has been found in the cord, there were apparently no clinical manifestations to suggest any disease of the nervous system. It must be remembered, however, that in these cases the nature of the hæmatological disorder was recognized and, presumably, occupied the foreground of the clinical picture. Consequently, in the absence of gross paralytic signs, it is possible that certain minor neurological abnormalities, as slight degrees of cutaneous, postural or vibratory sensibility, may have escaped detection, and the severity of the general condition may have masked a weakness or ataxy of the legs with alterations in the reflexes. The routine investigation of the central nervous system in all cases of leukæmia may in the future settle this vexed question.

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PLATE IV.

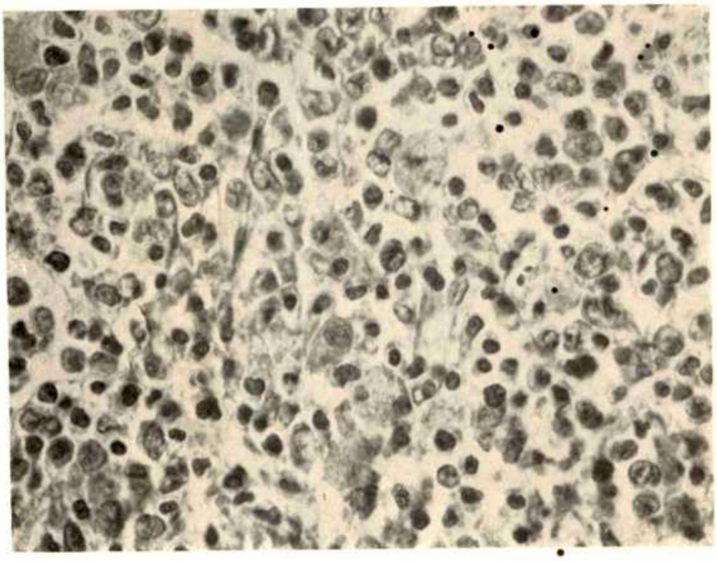

FIG. 1.

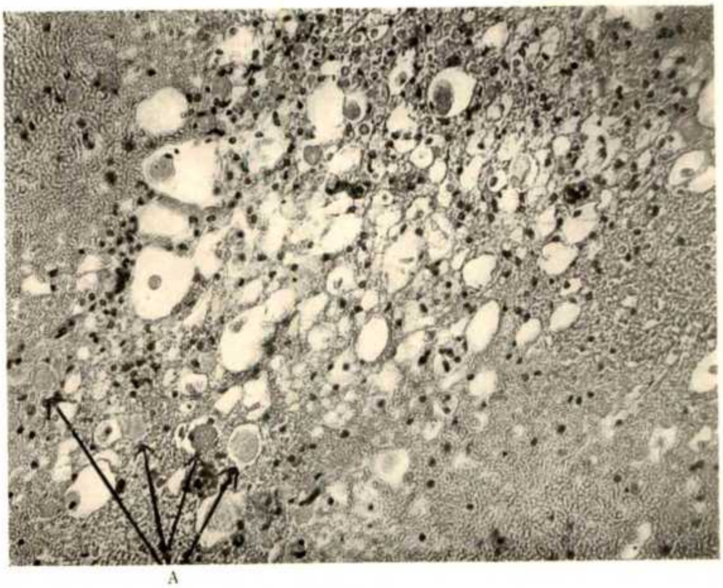

FIG. 2.

To illustrate paper by Macdonald Critchley and J. Godwin Greenfield.

PLATE V.

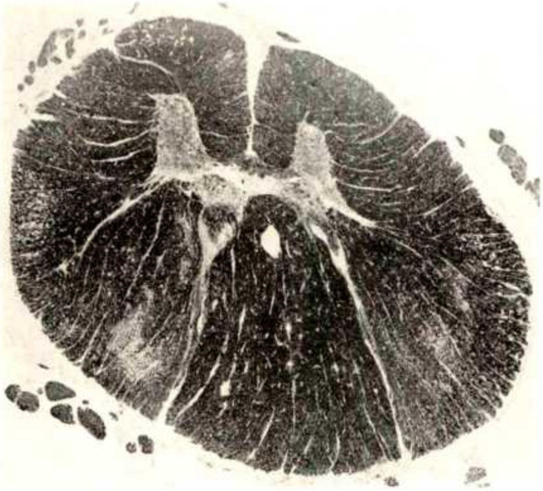

FIG. 3.

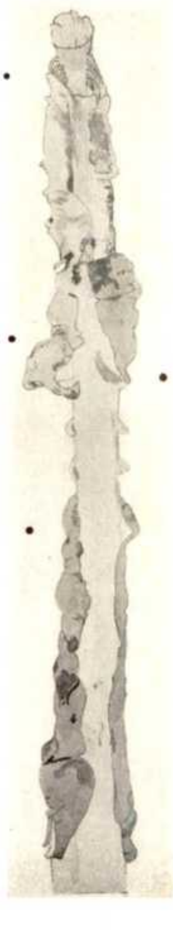

FIG. 5.

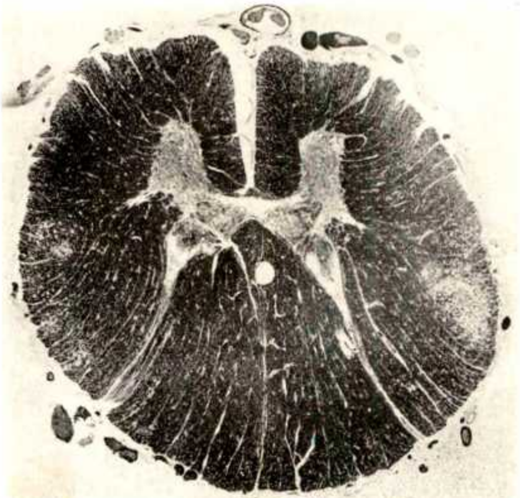

FIG. 4.

To illustrate paper by Macdonald Critchley and J. Godwin Greenfield.

PLATE VI.

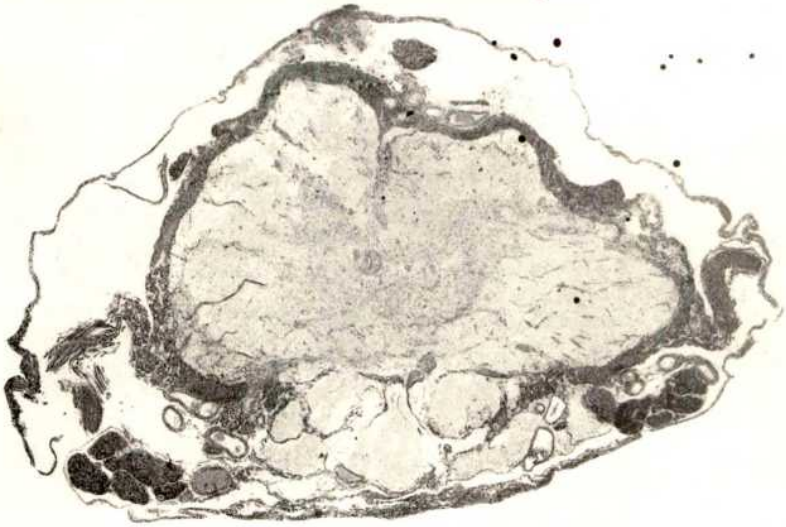

FIG. 6.

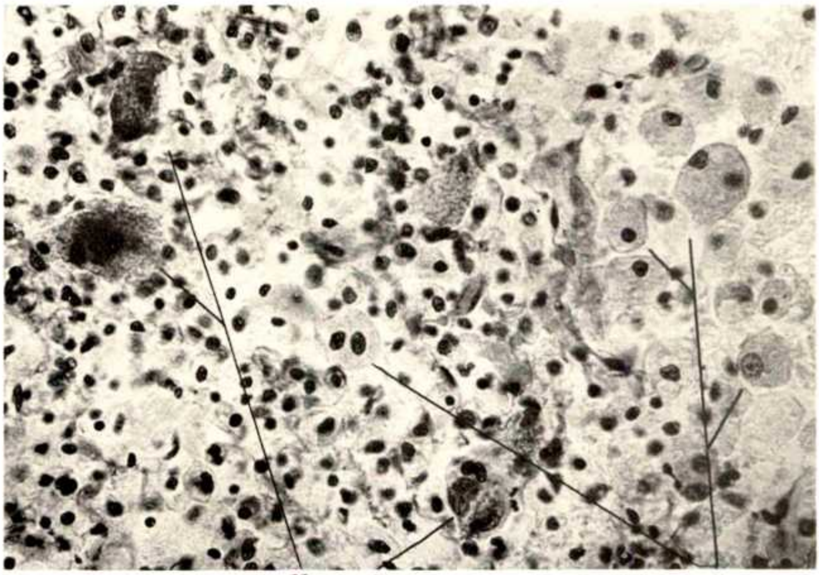

FIG. 7.

To illustrate paper by Macdonald Critchley and J. Godwin Greenfield.

DESCRIPTION OF PLATES.

FIG. 1.—*Case* 1. Cellular infiltration in falx cerebri. Three types of cell are seen: (1) Small cells with a darkly staining nucleus; (2) cells with a larger vesicular nucleus; (3) cells with a large cell-body containing lipochrome granules.

FIG. 2.—*Case* 1. Area of rarefaction in lateral column of fifth thoracic segment. Note the swollen axis-cylinders both in the vacuoles and in the surrounding tissues (A).

FIGS. 3 and 4.—*Case* 1. Transverse sections of the cord at the levels of the fifth and ninth thoracic segments (Loyez myelin stain). Areas of rarefaction are seen at both levels in the antero-lateral tracts.

FIG. 5.—*Case* 2. Drawing of spinal cord to show the cellular masses enveloping the dura mater.

FIG. 6.—*Case* 2. Low-power view of lower thoracic cord in transverse section. There is great thickening of the pia mater, except over the dorsal surface where it is broken through. The arachnoid is thickened in this position but not elsewhere.

FIG. 7.—*Case* 2. High-power view of the same section in the region of the ventral horn. The remains of three large nerve-cells are seen as nucleated granular masses (N). Elsewhere only fat-granule cells are present (G).

A CASE OF ARTERIOVENOUS ANEURYSM WITHIN THE BRAIN.

BY A. GURNEY YATES, M.D.,

AND

C. G. PAINE, M.B.

(*From the Pathological Department, University of Sheffield.*)

THE following case belongs to a group of intracranial vascular abnormalities to which Dandy has called attention in two recent articles [1], [2]. It presented somewhat striking clinical features, and the pathological changes subsequently found suggest a developmental origin.

W. Y., male, aged 32, was admitted to Fir Vale Hospital, Sheffield, on September 23, 1929. He complained of headache, defective vision and weakness on the right side.

History.—After a period of active service in France he returned to England in 1918, when he began to notice some weakness in the right arm and leg and slight intermittent headache. The onset was gradual. The symptoms at first were very slight. They slowly became worse, but he continued to do light labouring work until 1924, when he became unemployed. By this time the headache was almost continuous, with periodic severe exacerbations. It was worse in the early morning, and during severe attacks he had difficulty in speaking. At times he could not express what he wanted to say, and sometimes he found himself using the wrong word. His memory was poor, and his temper uncertain; at times he was quarrelsome and violent.

During the few months before admission to hospital, the pain in the head became more severe; it was localized in the left frontal region, behind and above the left eye, and it radiated down the left side of the face. Vision began to fail, the gait became much worse and there was a tendency to fall to the left. There were no fits of any kind and no vomiting, but frequent attacks of giddiness were complained of.

On admission to hospital the patient was mentally dull and at times slightly aphasic. The outstanding symptom was pain in the head. The sense of smell was normal on both sides. There was slight proptosis of the left eye. The pupils reacted normally, but the right was larger than the left. There was no nystagmus. Examination of the visual fields showed a right homonymous hemianopia. There was no optic neuritis, and the right disc was normal. The left disc showed no swelling and its outlines were clear, but the veins were enormously distended, and at the periphery, in the upper nasal quadrant, there was a small aneurysmal dilatation. On one of the arteries near the disc were three tiny bead-like dilatations separated by constrictions. (Fig. 1.) The appearance of the veins when first seen was more striking than is actually shown in the picture, perhaps because the patient was lying down, whereas when the artist drew the fundus he was sitting upright in a chair. The ocular movements were normal in all directions. The fifth nerve was normal except for the pain which spread downwards over the left cheek. There was slight weakness of the lower part of the left face. The other cranial nerves were unaffected. The right arm was paralysed and spastic in flexion. All the deep reflexes were increased. There was no sensory loss. The right leg was spastic and its movements impaired. All deep reflexes were increased and the plantar reflex was extensor. There was a partial loss of sensation in the foot. The left face, arm and leg were normal.

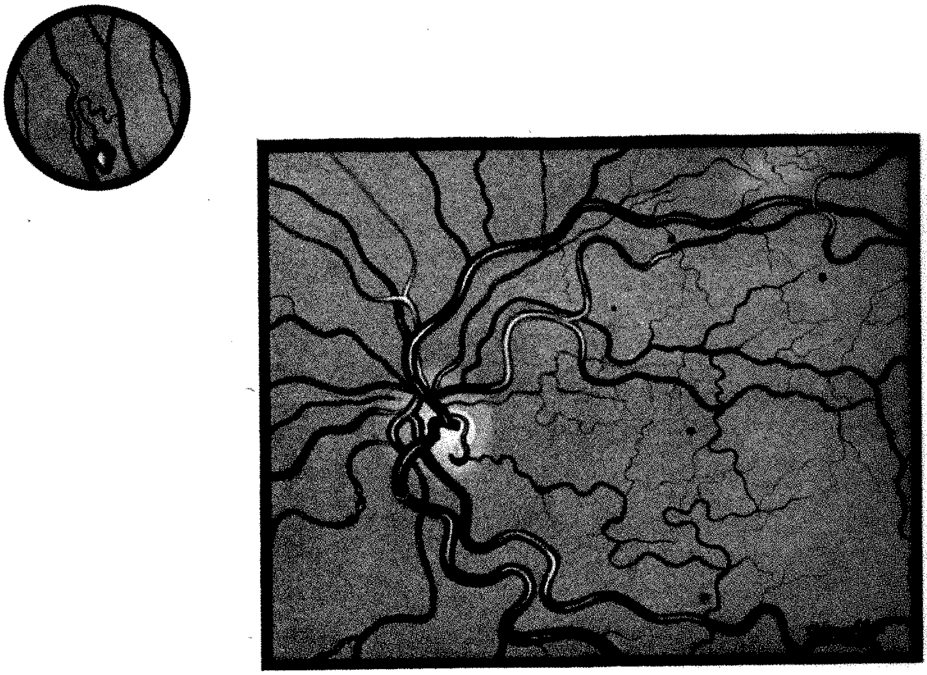

FIG. 1.

The only other physical sign was a blowing systolic murmur heard over the greater part of the head. It was loudest on the left side of the forehead, but it could be traced over to the right side, over both malar bones, and over the vertex nearly to the occipital region. There was no cardiac hypertrophy; the systolic blood-pressure was 110, and the diastolic 85. All other organs were normal.

The condition was thought to be an intracranial vascular lesion of the left cerebral hemisphere involving both the motor and visual paths, and in view of the severity of the symptoms, and particularly of the pain which was increasing, an operation was decided upon. Mr. Brockman exposed the brain in the left fronto-parietal region in the hope of finding an afferent vessel passing to the lesion. Several enormously dilated veins were seen running over the surface of the brain. They were dark in colour and did not pulsate. Unfortunately the patient died before the operation had proceeded very far.

Post-mortem examination.—There was a hæmorrhagic effusion beneath the site of the dural incision. On removal the brain weighed 46 oz. There was a very definite pressure cone in the region of the medulla and inferior part of the cerebellum, and this was evidently the immediate cause of death. The left side of the brain was smaller and the convolutions appeared somewhat atrophic when compared with the right side, especially in the region of the left occipital lobe.

The most remarkable feature externally was a series of abnormal venous channels engorged with blood. One venous channel passed from the left lateral sinus across the dural space to reach the left occipital pole, where it ramified over the occipital lobe, smaller venous channels occupying the sulci of the cortex in this region. Some of the branches penetrated the substance of the occipital lobe where their course was subsequently traced.

From the left Sylvian fissure ran a large, distended, thin-walled blood-vessel, corresponding to the superficial Sylvian vein. This passed downwards, backwards and inwards to empty into a large venous space immediately above, and communicating with, the cavernous sinus, which was grossly distended. A large torturous and distended venous channel ran from here backwards, close to the under surface of the brain, and passed lateral to the fifth nerve between the point of its emergence from the brain-stem and the Gasserian ganglion. At a point where it crossed superior to the posterior cerebral artery it was joined by another large venous channel which communicated anteriorly with the distended left superficial Sylvian vein, which passed over the antero-inferior surface of the left temporo-sphenoidal lobe.

After receiving this tributary the vessel continued its course backwards lateral to the general line of emergence of the cranial nerve-roots, skirting the side of the mid-brain, until it reached the region of the posterior portion of the splenium of the corpus callosum. A large communicating vessel branched from it here and ran inwards to join the vein of Galen, which was also greatly enlarged. Subsequently, the vessel passed backwards and entered the substance of the brain through the left calcarine fissure, where it broke up into a number of smaller vessels, finally opening into numerous venous spaces within the substance of the occipital lobe and giving this part of the brain an appearance somewhat resembling that of a cavernous hæmangioma. The penetrating branches of the venous channel from the left lateral sinus to the occipital pole also divided up within the substance of the brain and joined this "hæmangiomatous" area within the occipital lobe. Thus a direct venous communication extended from the cavernous sinus anteriorly to the left lateral

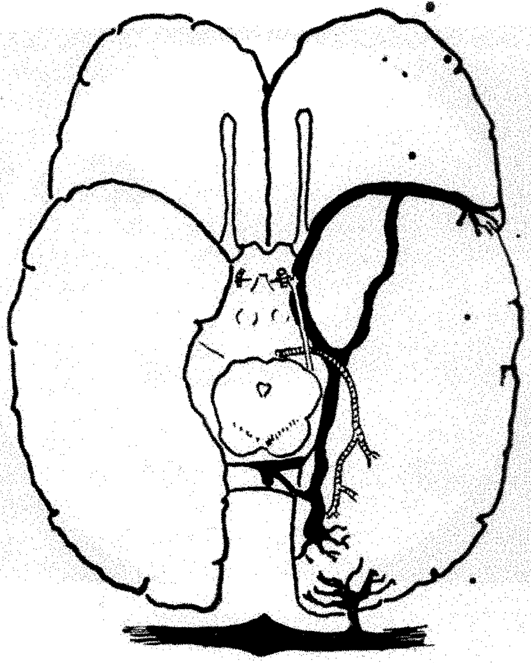

FIG. 2.—Diagram of base of brain showing the abnormal vascular channels.

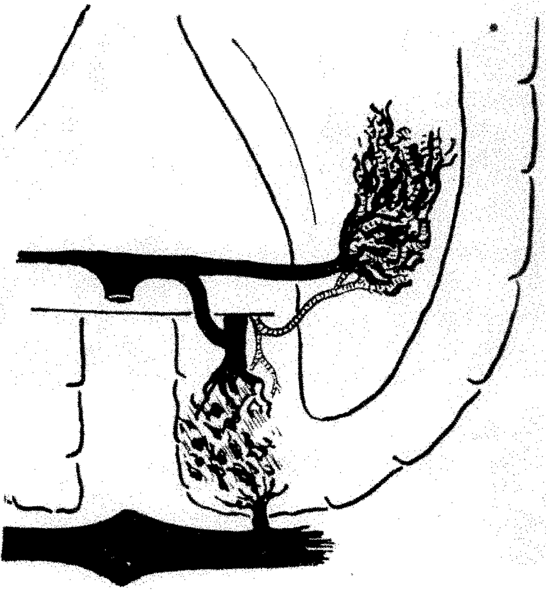

FIG. 3.—Diagram of section through left lateral ventricle and left occipital lobe, showing vascular abnormalities in the choroid plexus and occipital region.

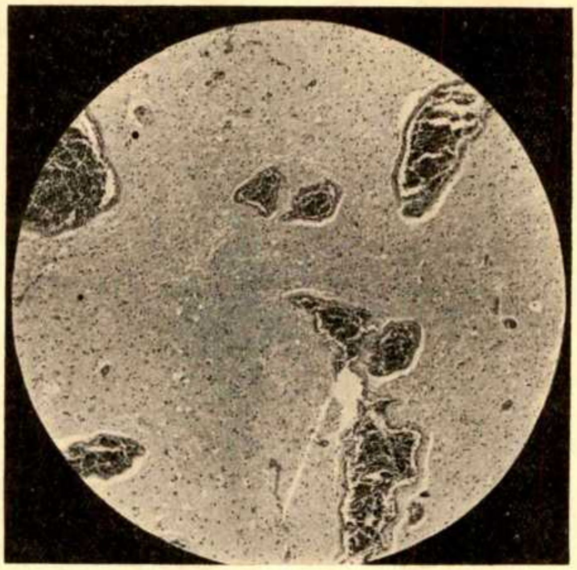

FIG. 4.—Photomicrograph of the occipital cortex, showing large numbers of thin-walled venous channels.

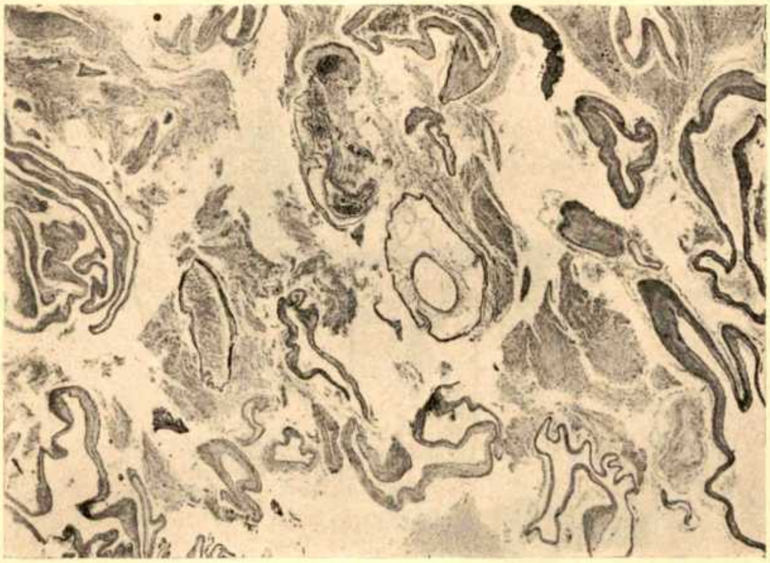

FIG. 5.—Photomicrograph of section through the choroid plexus.

sinus posteriorly, the direct communication being established by means of the large number of venous spaces within the substance of the occipital lobe.

A diagrammatic representation of the condition described is shown in figs. 2 and 3.

A photomicrograph of the occipital cortex is shown in fig. 4.

The arterial system also showed slight changes. The arrangement of the circle of Willis was normal. The basilar artery at its point of bifurcation divided into left and right posterior cerebral arteries, but the cross-sectional area of the left posterior cerebral artery was about three times that of the right. The posterior choroidal branches and the calcarine branch of this artery were correspondingly enlarged. A similar relationship was shown between the left and right veins of Galen, and whereas on the right side the choroid plexus of the lateral ventrical appeared normal, that on the left side was replaced by a twisted, worm-like mass of dilated vessels.

This condition is shown in diagram in fig. 3.

Fig. 5 is a photomicrograph of a section through the vascular mass which replaced the left choroid plexus.

The lateral ventricle on the left side was dilated and there was some general thinning of the surrounding cerebral cortex. The right ventrical appeared normal. In view of the fact that no obstruction to the free communication between the two ventricles could be found this dilatation of the lateral ventricle remains unexplained.

In order to exclude any direct arterio-venous communications that might have been overlooked in the dissection, the arterial and venous systems were injected in turn with an opaque paste and X-ray photographs taken. No such communication was found.

DISCUSSION AND EMBRYOLOGICAL CONSIDERATIONS.

Dandy, who has described a small series of similar cases, suggested that the condition is probably a congenital abnormality. An attempt has been made, therefore, to correlate the findings in this case with the development of the venous system of the brain and a possible explanation of the abnormal conditions is advanced.

Before dealing with the abnormalities of venous development in this case, brief reference must be made to the stages of normal development of the cerebral venous system.

At the base of the primitive brain-stem there exists a single channel, a continuation forwards of the anterior cardinal vein. The posterior end of this forms the jugular bulb and part of the lateral sinus, and the anterior end dilates to form the primitive cavernous sinus. Into this primitive cavernous sinus blood drains from the anterior part of the developing brain, more especially from a plexus of veins representing the superficial Sylvian group of veins. (Fig. 6, *a*.)

This primitive channel is reduplicated by another vessel passing forwards lateral to the otic vesicle, which joins behind and in front with the anterior cardinal vein. This channel is the vena capitis lateralis. With the growth of this secondary channel there is a subsequent atrophy of that part of the anterior cardinal vein between the jugular bulb and the cavernous sinus. (See fig. 6, *b*.) From the primitive cavernous sinus there grows forwards, upwards and then backwards, with the development and growth of the neopallium, a prolongation which subsequently

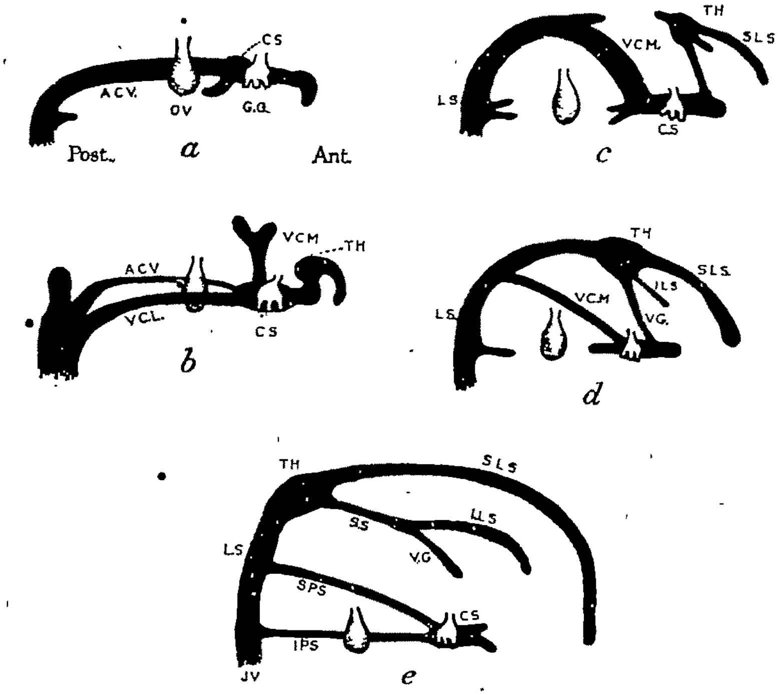

FIG. 6.—Developing venous system (modified from Quain's Anatomy). A.C.V., anterior cardinal vein. C.S., cavernous sinus. G.G., Gasserian ganglion. I.L.S., inferior longitudinal sinus. I.P.S., inferior petrosal sinus. J.V., jugular vein. L S., lateral sinus. O.V., otic vesicle. S.L.S., superior longitudinal sinus. S.P.S., superior petrosal sinus, S.S., straight sinus. T.H., torcula Herophili. V.C.L., vena capitis lateralis. V.C.M. vena capitis medialis. V.G., vein of Galen.

forms the superior longitudinal sinus and the torcula Herophili. The residual venous channel between the primitive torcula Herophili and the cavernous sinus represents the vein of Galen. (Fig. 6, *c*.)

Normally, with the development of secondary venous communications by which drainage may take place, i.e., the formation of a junction between the torcula Herophili and the jugular bulb, and the upward growth of the vena capitis medialis which will later represent the superior pretosal sinus, the primary blood-channels, more especially that part of the anterior cardinal vein between the jugular bulb and cavernous sinus, and also the vena capitis lateralis, atrophy and disappear. The primitive vein of Galen, being able to drain into the lateral sinus via the torcula Herophili, also loses its connection with the anterior cardinal vein. The stages of this evolution are shown diagrammatically in figs. 6, *c*, *d*, *e*. The condition shown in fig. 6, *e* corresponds roughly to the adult venous drainage system.

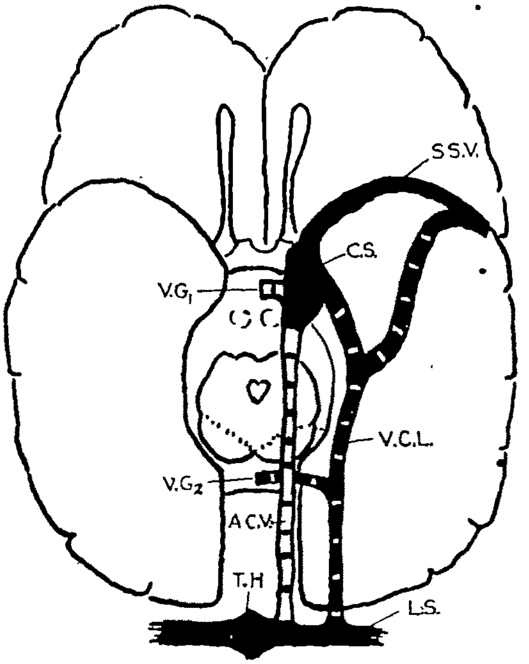

FIG. 7.—Vessels shown in continuous black are normally present in adult life. Dark interrupted lines indicate veseels that disappear during development normally but which have persisted in this case: light interrupted lines indicate fœtal vessels that have disappeared. A.C.V., anterior cardinal vein. C.S., cavernous sinus. L.S., lateral sinus. S.S.V., superficial Sylvian vein. T.H., torcula Herophili. V.C.L., vena capitis lateralis. V.G 1, vein of Galen—site during fœtal life. V.G.2, vein of Galen—site due to persistence of left vena capitis lateralis.

These details of development throw a definite light on the abnormal conditions present in the case which is described here. It is suggested that the large venous channel skirting the side of the mid-brain and joining anteriorly with the cavernous sinus is a persistent left vena capitis lateralis. Instead of draining straight into the lateral sinus and jugular bulb, it breaks up into a number of venous channels within the substance of the left occipital lobe. These re-assemble and then flow into the lateral sinus by the vessel crossing the dural space. The large vessel lying in the Sylvian fissure is merely the dilated and distended counterpart of the normal superficial Sylvian vein; while the vessel joining the superficial Sylvian vein to the persistent vena capitis lateralis is a survival of the primitive superficial cerebral venous plexus found in that region.

The connection between the vein of Galen and the vessels at the base of the brain is usually lost. In this case, however, it has persisted. But with the growth backwards of the cerebral vesicles there is a tendency for the point of connection between the vein of Galen and the vessels at the base of the brain to be drawn backwards. This has apparently happened, the passage being made along the vessel that has persisted, i.e., the vena capitis lateralis. Thus a communication between the vein of Galen and the vena capitis lateralis is explained. A diagrammatic representation of this is shown in fig. 7.

The reason of the persistence of these venous channels is problematical. It is suggested that there is, in this case, an absence, or minimal development, of a capillary bed, between the arterial and venous systems in the areas affected. The capillary bed acts as a buffer between those two systems, and the persistence and dilatation of these abnormal vessels is probably in the nature of a compensatory mechanism to deal with the abnormally large quantity of blood that is uncontrolled because of the absence of a "buffer" action of a capillary bed.

As to the classification of this lesion, it will be remembered that Ribbert [3] regards hæmangiomata as arising in rudiments of displaced fœtal tissue which are destined to form blood-vessels. From this rudiment they grow independently, thus explaining the apparent independence of the intra-hæmangiomatous circulation from the surrounding capillary circulation. In this case the vascular mass is dependent upon the normal circulation, and this fact in itself does not permit of its classification with the hæmangiomata.

Dandy has suggested the term "aneurysm by anastomosis" for such conditions, and this term not only fits this case, but also gives a very clear indication of the underlying pathological process.

It gives us great pleasure to acknowledge our indebtedness to Dr. M. A. MacConnaill of the Anatomy Department, The University, Sheffield, for his assistance with the embryological details in this case.

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[2] *Idem. Ibid.*, 1928, **17**, 715.
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DIABETES INSIPIDUS.

BY ELIZABETH COWPER EAVES, M.D.,

Lecturer in Physiology, University of Sheffield, and Honorary Neuropathologist, South Yorkshire Mental Hospital, Wadsley, Sheffield.

DIABETES INSIPIDUS is a comparatively rare condition; in a statistical examination Fitz found only fourteen cases per 100,000 patients. In the South Yorkshire Mental Hospital, which contains about 1,800 patients, many suffering with organic disease of the brain, one instance only has been recognized within the last six years.

The pathology of the condition is confusing. Many physiologists assume, owing to the properties of extracts of the posterior lobe of the pituitary and the undoubted fact that their administration has alleviated the symptoms in many reported cases, that the pituitary is necessarily involved. On the other hand, there is experimental and clinical evidence that a small lesion in the region of the tuber cinereum may bring about diabetes insipidus.

Polyuria may occur, but is not invariably associated, with tumours of the pituitary or in adjacent portions of the brain, and after cranial injuries, particularly fractures of the base of the skull. Syphilitic meningitis is an occasional cause. With or without obesity it may be a sequel of epidemic encephalitis.

The literature on the clinical and experimental aspect of diabetes insipidus is very large. Reference to much of this is given in papers by Kennaway and Mottram [10], Geiling [8], Bailey [2], Trendelenburg [13]. Little is known of the pathology of diabetes insipidus occurring in man, and in comparatively few instances has a complete examination been made both of the hypophysis and brain.

The first two cases to be described differ very widely from each other in their ætiology, Case 1 being probably due to a congenital defect and Case 2 being post-encephalitic.

CASE 1.—DIABETES INSIPIDUS WITH INFANTILISM.

A man, aged 21, a patient of Dr. Mathieson, suffered from epileptic fits from the age of 9. He was admitted to the South Yorkshire Mental Hospital two years before death. He had frequent severe epileptic fits, always appeared dazed and suffered greatly from headaches. His appetite was large, he was always thirsty and he passed large quantities of urine. He was mentally defective, being unable to answer simple questions. The fits became progressively worse, and he finally died from exhaustion following numerous epileptic seizures.

He had had scarlet fever twelve months, and rheumatism eight years, before admission. His father is an epileptic.

Condition.—Although aged 21, he had the appearance of a boy of 10. He was very undersized, his weight being 5 st. and his height 4 ft. 9 in. The physical condition was rather similar to the Lorain type of infantilism. There appeared to be nothing unusual in the general appearance of the limbs. The head was large and contrasted with the small size of the face. The abdominal organs showed no abnormality. The testicles were very small.

No definite abnormality was detected in his nervous system. It was impossible to test sensation owing to his mental condition. Nothing abnormal was observed in the eyes. His pupils were equal and regular, and contracted directly and consensually to light and on accommodation.

The cardiac impulse was diffuse and a mitral systolic murmur was present. There was no arteriosclerosis. The urine had a specific gravity of 1005, and contained no abnormal constituents. Large quantities were passed.

Post-mortem examination.—The bones of the skull were unusually thick. The brain weighed 59 oz. The ventricles were normal. There was no excess of cerebrospinal fluid.

The pituitary.—The pituitary was not more than about half the normal size and of unusual form. In some parts it appeared to be constricted by connective tissue (plate VII, fig. 1). The cleft between the lobes seemed unusually wide considering the age, and was similar in this respect to that of a child. There was a cyst in the anterior lobe (fig. 2) and in the posterior lobe a partial division by a collection of small cells.

The cells of the anterior lobe were small and nearly all chromophobe. A few basophiles were found, but the number of acidophiles was extremely small, only 2·1 per sq. mm. in sections 4 μ thick.

The pars intermedia was also small; its cells were ill-formed and their cytoplasm scanty, in many cases the small nucleus almost filling the cell. In the pars nervosa the neuroglial cells were less than half the normal size, and the tissue seemed unusually vacuolated.

It seemed of interest to compare this pituitary with that in infantilism of a different type. Dr. S. J. Cowell kindly allowed the writer to examine the pituitary from a case of renal infantilism in a boy aged 16. This only weighed 0·34 grm., less than normal, but the acidophiles, although small and apparently few in number, averaged 700 to 900 per sq. mm., indicating a certain degree of activity.

The nervous system.—The most remarkable feature was the large size of the brain and its firm consistency. There was no obvious macroscopic abnormality, indeed it seemed a particularly well-developed brain, contrasting very much with the mental condition of the patient.

All parts of the central nervous system were examined microscopically. The main changes were those usually observed where the patient had died from status epilepticus, viz., chromatolysis of the nerve-cells and slight increase in the neuroglia. There was no degeneration of tracts, which appeared completely myelinated in Weigert-Pal preparations, and the various nuclei were very well developed. The medium-sized blood-vessels were slightly thicker than normal. In the hypothalamic region there were no lesions of any kind, apart from changes due to status epilepticus—similar to those in the rest of the nervous system. There was no destruction of nerve-cells in the substantia nigra nor in any other part of the mid-brain.

Although histologically the brain appeared to be well developed, it was thought that chemical analysis might reveal some abnormality. The amount of phosphorus was remarkably low, being only 0·204 grm. (expressed as P_2O_5) in 100 grm. of cerebral cortex. The amount of phosphorus varies normally from 0·35 to 0·4 grm. The amount of calcium was probably within normal limits—4·8 mg. per 100 grm. of cerebral cortex.

CASE 2.—POST-ENCEPHALITIC DIABETES INSIPIDUS.

A man, aged 29 at death, was admitted to Lodge Moor Hospital in 1924 under the care of Dr. A. G. Yates, with acute epidemic encephalitis. He recovered and was discharged. Subsequently, he began to complain of mental depression, had outbursts of temper, could take no interest in anything and had thoughts of suicide. Early in 1926 he complained of thirst and headache and began to get fat. Exact weights are not available, but he very obviously put on a great deal of weight and drank enormous quantities. In April, 1926, he was admitted to the Firvale Infirmary Mental Ward. He was then mentally degenerated, slept a great deal, and had frequent epileptiform attacks in which he was unconscious, bit his tongue and was incontinent. There was a faint trace of Parkinsonism, but this never became at all marked. Epileptic fits and polydipsia continued until August 15, 1926, when he died suddenly in an epileptic seizure.

The quantity of urine was always very large—in one day 178 oz. (about 5,038 c.c.), another time 6,300 c.c. Its specific gravity was 1005, but it contained no abnormal constituents.

The pupils reacted to light, but the left was larger than the right. The abdominal and plantar reflexes were normal. The Wassermann reaction was negative.

Post-mortem.—The stomach was enormously dilated, but all the other organs appeared normal, including the kidneys.

The pituitary.—The pituitary was larger than normal. It weighed 0·75 grm. On making a vertical antero-posterior section, a collection of colloid could be seen between the anterior and posterior lobes (fig. 3).

Microscopically, in the anterior lobe the acidophiles seemed fairly abundant but slightly smaller than usual, and there were islands of hyperplasia. The basophiles were fairly numerous in some areas.

In the pars intermedia there were numerous vesicles or cysts of varying sizes containing colloid, some of which possessed a definite cellular wall. In one large vesicle the lining cells appeared to be ciliated. There were also many islands of cells enclosed by connective tissue which occasionally contained colloid towards the centre. There appeared to be here some hyperplasia of the pars intermedia. Some of the cells were vacuolated and more chromophobe than normal. The colloid varied in its staining properties, for example with Mallory's aniline blue-orange G part of it stained yellow, part blue, signifying some difference in reaction.

In the pars nervosa the neuroglial cells and fibres seemed well developed. Clumps of bright yellow pigment were abundant, also ill-defined feebly staining colloid masses at intervals. There was a tendency to accumulation of hyaline material round the vessels. In some areas the neuroglial fibres were unusually widely separated as though there had been some distension by secretion.

The nervous system.—There was no wasting of the brain, which weighed 48 oz.

There was no percentage diminution of phosphorus compounds as is invariably found in degenerative conditions of the nervous system, such as general paralysis of the insane and in Huntington's chorea (0·405 P_2O_5 in 100 grm. of cerebral cortex). Chemical analysis indicated an increased calcium content. In the frontal cortex the amount was 9·8 mg. in 100 grm., the average figure at the age of the patient being from 4 to 4·5 mg. In other regions than the cortex, as in the hypothalamic region and throughout the brain-stem, there was even greater increase in calcium if one could judge by the histological appearance.

All parts of the nervous system were examined histologically, and as far as possible serial sections of the hypothalamic region were made. The most striking feature was the condition of the blood-vessels. These were thickened, and spaces existed round them. This was not due to fixation, which was otherwise fair. Hæmorrhages were not frequent, but a small one was found in the hypothalamic region immediately anterior to the corpus mammillare; it did not involve any nucleus of nerve-cells.

There was no obvious degeneration of tracts in Weigert-Pal preparations. Chromatolysis of nerve-cells and neuronophagia were present throughout the whole nervous system, but it was remarkable that these changes were notably less than in most of the nine other cases of chronic epidemic encephalitis that I have examined.

In the hypothalamic region all the nerve-cells exhibited chromatolysis, and some were in process of destruction and surrounded by glia cells (fig. 4.) As particular importance has been ascribed to a lesion of the ventral nucleus as a causative factor in the production of polyuria (Camus and Roussy [4], Bailey and Bremer [3]), an attempt was made to compare the amount of change in the nerve-cells of this nucleus with that in the periventricular nuclei, the nuclei of the optic tracts, the accessory supra-optic nuclei and the corpora mammillaria, but it was found to be impossible.

In the substantia nigra many nerve-cells remained, although few could be considered normal. Contrasting these findings with those in nine other brains from cases of epidemic encephalitis in which there was no diabetes insipidus, it is to be emphasized that in some of the latter the destruction of cells in the hypothalamic region was so great that the different nuclei could not always even be identified, and in some of these brains the ventral nucleus of the tuber appeared to have suffered more than the other nuclei. In the majority of cases only small clumps of pigment remained in the substantia nigra to mark the original site of the cells of this structure.

The liver, in spite of the obesity, contained no stainable fat and appeared otherwise normal, except for a slight increase of tissue around the portal canals. Owing to post-mortem changes in the pancreas, no statement can be made about it.

CASE 3.—TRANSITORY POST-ENCEPHALITIC DIABETES INSIPIDUS.

G. C., a man aged 17 at the outset of his illness, a patient of Professor Hall at the Sheffield Royal Hospital, had epidemic encephalitis in January, 1922, when he was very drowsy for eight or nine weeks. In May, 1925, polydipsia and polyuria developed, the specific gravity of the urine being then about 1002 and the total daily amount about ten litres. He was treated with pituitrin by Dr. Imrie, with the result that the polyuria decreased (Tingle and Imrie [12]). By August, 1926, thirst and polyuria had disappeared, but tremors, rigidity and oculogyric crises were present. He continued to lose weight. He became bad-tempered and violent occasionally.

When examined in June, 1929, he was markedly Parkinsonian, helpless and very thin. He was usually quiet and orderly, but at intervals he was difficult to manage. The patient said he had terrible attacks in which his eyes turn up. These attacks were stated by the Charge Nurse to last sometimes as long as two days. He was not now troubled by excessive thirst.

The fundi appeared normal. The pupils reacted sluggishly to light. There was paresis of the right external rectus muscle and bilateral weakness of the facial muscles, more marked on the right side. Nothing abnormal was observed in the other cranial nerves. The right pupil dilated more to shade than the left. Sweating was considerable. Tremors were present in the ocular muscles, tongue, lips and in the limbs, and there was great rigidity. The specific gravity of the urine varied between 1012 and 1018. It contained no albumin nor sugar. The total quantity in twenty-four hours was about 60 oz. (1,698 c.c.).

CASE 4.—TRANSITORY DIABETES INSIPIDUS WITHOUT NERVOUS DISEASE.

Mrs. C., a woman aged 29, under the care of Professor Hall, was admitted to the Sheffield Royal Hospital in July 1908, suffering from great thirst and polyuria. These symptoms dated from the birth of her ninth child three months previously. During the three weeks in hospital the average daily amount of urine was 3,500 c.c. The specific gravity varied from 1003 to 1006, and there were no abnormal constituents. In September, 1915, she seemed much better, but still had abnormal thirst: for example, she would usually drink about a quart of water in the night. In February, 1929, more than twenty years after the onset of diabetes insipidus, she was quite well, and no longer had either polydipsia or polyuria. The specific gravity of the urine was about 1015.

Some Abnormalities of the Posterior Lobe of the Pituitary without Polyuria.

(*a*) *Hyperplasia of the pars intermedia and of the pars tuberalis*.—The appearances, seen in the posterior lobe of the pituitary in a case of acromegaly under Professor Hall at the Sheffield Royal Hospital, seem of some importance. The patient had never been known to have diabetes insipidus. This pituitary weighed 2·4 grm. In addition to the usual hyperplasia of the pars anterior, there was also a hyperplasia of the pars intermedia, such as the present writer has not previously seen in any pituitary. The pars nervosa was very small, but the pars tuberalis seemed unusually large.

Hyperplasia of the pars intermedia was also found in a pituitary from a case of epidemic encephalitis in which polyuria had not been present. This differed from Case 2, in that in the latter the pars intermedia was divided into islands by increased connective tissue.

(*b*) *A tumour involving the pars nervosa*.—This was a case of Dr. E. F Skinner in which a pituitary tumour had not been suspected. Macroscopically, the whole posterior lobe appeared to be involved by a tumour which extended round both sides of the pituitary. Microscopically, however, the pars nervosa alone was found affected, the pars intermedia being to some extent hyperplastic.

DISCUSSION.

There are two main theories advanced to explain diabetes insipidus.

(*a*) *The endocrine theory*.—Posterior lobe extract has both a diuretic and anti-diuretic effect, and consequently there are two variations of this theory: (1) that polyuria is due to an increased secretion of hormone; (2) that it is brought about by a diminution in the available amount of hormone either owing to a deficient production or interference with absorption. The balance of evidence is that the effect of posterior lobe extract is mainly anti-diuretic in human beings. The site of origin of an active extract is probably the pars intermedia rather than the pars nervosa. It has been shown earlier that neither hyperplasia of the pars intermedia nor of the pars tuberalis is associated with polyuria.

(*b*) *The nervous theory*, as propounded by some workers, excludes the pituitary from any share in the production of polyuria and ascribes the condition to lesions in the hypothalamic region [2], [3], [4].

A reconciliation of the two theories is possible. That there are actually nerve-fibres in the pituitary, except to the vessels, has been disputed owing to technical difficulties in their demonstration. M. M. Croll [6], however, has recently shown beyond doubt that in the rabbit the pars intermedia is very richly innervated (the references to previous work are given in her paper), and Greving [9] and Pines [11] have described tracts of fibres passing from the hypothalamic region to the hypophysis. A disturbance of function of the pituitary by interference with the nerve supply is therefore a possibility.

In Case 1 there was no definite lesion of the nervous system to account either for diabetes insipidus or for infantilism. Some workers, more particularly of the French school, have ascribed infantilism also to lesions in the hypothalamic region. The histological findings in the brain resembled those in other cases of macrocephaly (Anton [1] and Wigglesworth and Watson [14]), that is, there were few or no pathological changes apart from those usually found in epilepsy. There was no tumour of the pituitary to exert pressure on adjacent nerve-centres, but the pituitary was maldeveloped and there was histological evidence of under-activity, at any rate of the anterior lobe. The polyuria in this case must, therefore, be considered to be due to insufficient production of hormone by the pituitary.

In Case 2 the pituitary in no way resembles that in Case 1, as it was slightly larger than normal, and there was hyperplasia of the pars intermedia. Polyuria was not due to this hyperplasia, as will be obvious from a comparison with the acromegalic pituitary. Comparing this pituitary from Case 2 with those from other cases of epidemic encephalitis, the most important difference was the presence of a larger amount of colloid in the pars intermedia than in any of the others except one from encephalitis with obesity. There was the possibility of interference with absorption of hormone into the blood-vessels owing to their abnormal condition, and into the third ventricle owing to the increased calcium in the brain.

The mildness of the lesion in the hypothalamic region in Case 2, compared to the severity of the changes in other encephalitic brains, is in line with the clinical condition of Case 3 at different stages of the malady. In both Cases 2 and 3, diabetes insipidus occurred before the onset of definite Parkinsonism. The disappearance of polyuria in Case 3 was obviously not due to improvement of the condition of the nervous system, the changes in which were progressive. It may be attributed to the use of pituitrin, but although this substance had an immediate effect while it was administered, the effect was hardly likely to be permanent when it was withdrawn.

Transitory diabetes insipidus, with progressive disease in the nervous system, has been noted by Fulton and Bailey [7] in two cases. In one of these polyuria had been present for five or six years, but disappeared eight months before death. The tuber cinereum was involved by a tumour, and there was dense gliosis and only a few sparse surviving neurons. The hypophysis was normal.

In any consideration of the influence of the nervous system on the pituitary, it is generally assumed that if there is nervous control stimulation of a particular group of nerve-cells will bring about secretion. But the effect may be of an inhibitory rather than a secretory nature, and a mild lesion by stimulating such a centre may inhibit the secretion of the anti-diuretic hormone. That a ductless gland may be influenced by inhibitory impulses from the nervous system has been shown in the case of the islets of Langerhans of the pancreas by Clark [5].

Case 4 illustrates that transitory diabetes insipidus is not necessarily a symptom of a serious and progressive disease. There were never any neurological signs, and the condition followed pregnancy where there is even normally some alteration in the function of the pituitary.

CONCLUSIONS.

(*a*) Diabetes insipidus may be due to a transient affection of the pituitary, and this gland may recover its function completely.

(*b*) It may be present as a permanent condition owing to a more severe affection of the pituitary—as, for example, a congenital defect.

(*c*) Neither hyperplasia of the pars intermedia nor of the pars tuberalis of the pituitary causes diabetes insipidus.

(*d*) A relatively mild lesion in the hypothalamic region of the brain may bring about diabetes insipidus. It is suggested that this is due to stimulation of an inhibitory centre or tract to the pituitary, thus causing inhibition of secretion of the posterior lobe hormone.

(*e*) A severe lesion in the hypothalamic region of the brain—in contradistinction to a milder one—does not bring about diabetes insipidus—as was apparent in nine cases of chronic epidemic encephalitis.

The writer is indebted to Professor Hall for particulars of two of his cases and for the pituitary from his case of acromegaly; to Dr. A.

PLATE VII.

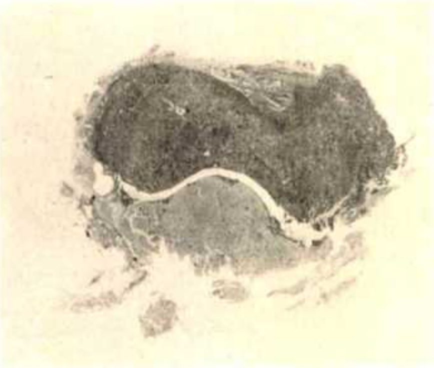

FIG. 1.

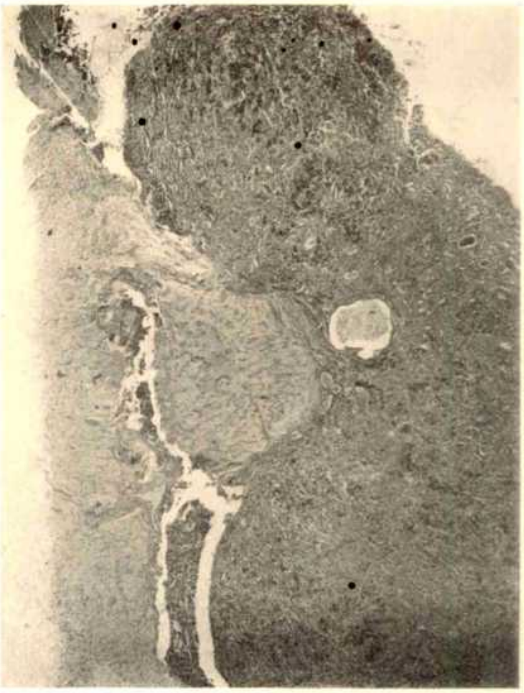

FIG. 2.

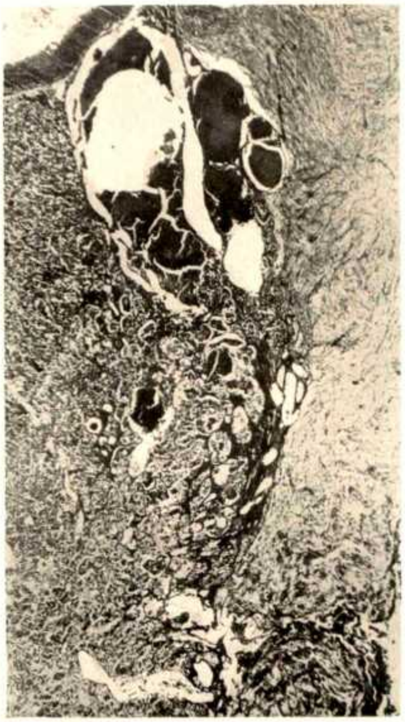

FIG. 3.

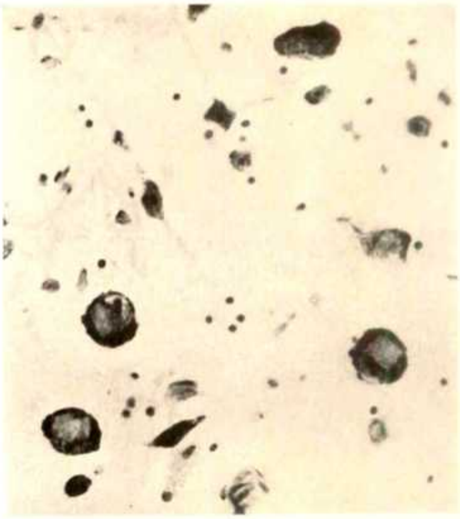

FIG. 4.

To illustrate article by Elizabeth Cowper Eaves.

G. Yates for permission to publish his case of post-encephalitic diabetes insipidus; and to Professor Leathes for some helpful criticism. She thanks Mr. C. Stewart and Mr. R. Stewart for assistance with photomicrography.

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DESCRIPTION OF PHOTOMICROGRAPHS. PLATE VII.

Fig. 1.—*Case* 1. Pituitary. × 5½. Antero-posterior section. The pituitary is of abnormal form and is constricted in one place by connective tissue. The cleft between the lobes is unusually patent for the age.

Fig. 2.—*Case* 1. The pituitary at the junction of the anterior and posterior lobes. × 17½. There is a cyst containing degenerative material in the pars anterior, and the pars nervosa is partly divided by small cells.

Fig. 3.—*Case* 2. Antero-posterior vertical section of the pituitary. × 18. (Fuchsin and Mallory's aniline blue orange G.) Large vesicles containing colloid. The amount of connective tissue at the junction of the two lobes is increased and divides up the slightly hyperplastic pars intermedia into islands.

Fig. 4.—*Case* 2. Nerve-cells in the hypothalamic region. × 280. The nucleus of the cells is eccentric in position. The centre of the cells contains no Nissl granules, the edges stain darkly with methylene-blue. Some of the cells are being destroyed.

THE PITUITARY AND HYPOTHALAMIC REGION IN CHRONIC EPIDEMIC ENCEPHALITIS.

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AND
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It is well known that in epidemic encephalitis symptoms occasionally occur similar to those which have been attributed to affections of the pituitary or to lesions in the hypothalamic region of the brain. Obesity, sometimes approximating to Fröhlich's type, and diabetes insipidus, are the two more common of the symptoms with a debatable hypophyseal or nervous origin, but hypophyseal infantilism and acromegaly have been also described, but they are very rare.

Obesity, or some unusual increase in weight, seems to be commoner than diabetes insipidus, though the two symptoms may be present in the same case. Exact statistics as to the actual proportion of cases which have diabetes insipidus do not seem to be available but a review of the literature makes it evident that this rare condition occurs with greater frequency in epidemic encephalitis than in any other disease. There is considerable variation in the percentage figures given by different observers with regard to the number of cases in which there is obesity. For instance, Grossman [8] who examined a series of eighty-nine cases, mainly children, found it in 15 per cent.; Duncan in a series of eighty-three cases in about 8 per cent. Professor Hall tells us that these figures are higher than he has found. A number of instances of post-encephalitic obesity are cited in the monographs by A. J. Hall [9] and F. Stern [16].

The occurrence of post-encephalitic infantilism and acromegaly—although we have only found one example of each in the literature—is of great interest because the pituitary must have been affected. Bremer [3] observed acromegaly to develop quickly after a typical attack of epidemic encephalitis, and Parhon, Ballif and Mârza [15] have described a case of post-encephalitic infantilism with diabetes insipidus.

Many patients with chronic epidemic encephalitis become very wasted, but the reason for this emaciation is not obvious. A variety of Parkinsonism, accompanied by severe wasting, has been described, but the two conditions are not necessarily associated as will be seen from a consideration of some of the ten cases described in this paper. It seems, therefore, worth considering if this cachexia is due to any change in the pituitary.

Disturbances of sleep are present in practically all cases of epidemic encephalitis at some time. The possibility that pathological drowsiness is due to hypofunction of the pituitary must be considered. It is common knowledge that lesions in the hypothalamic region may cause disturbances of sleep, and it is usually assumed that this is the cause in epidemic encephalitis without, however, there being definite proof.

Our attention was first attracted to the problem of the pituitary and the hypothalamic region in epidemic encephalitis because of the opportunity afforded to one of us to examine the pituitary and nervous system in a case of post-encephalitic diabetes insipidus. It was realized that in such a diffuse disease as epidemic encephalitis the fact that any definite pathological change was present in the pituitary or hypothalamic region did not necessarily indicate that these changes were responsible for any particular symptoms; and it seemed necessary to compare the appearances in this case of diabetes insipidus with those of the same structures in the brain of other cases of epidemic encephalitis in which this symptom was absent. It was also important to ascertain with what frequency and severity changes might exist in the hypothalamic region in the absence of any syndrome commonly attributed to a lesion in this area.

PREVIOUS WORK ON THE PITUITARY AND HYPOTHALAMIC REGION IN EPIDEMIC ENCEPHALITIS.

The paucity of pathological data is in rather striking contrast with the number of clinical instances of post-encephalitic hypophyseal syndromes. The pituitary has occasionally been examined in acute cases of short duration. Marie and Trétiakoff [13], who comment on the absence of information about the hypophysis in epidemic encephalitis, examined this structure in two acute cases in which drowsiness was a prominent symptom. They noted congestion but no pathological change which was not found in other conditions. Apparently the hypothalamic region was not examined.

Howe [11] described some pathological changes in four acute cases, and states that while the alterations in the pituitary are definite, there is no evidence that the course of the disease is influenced thereby. He considers, however, that many more cases should be investigated before definite conclusions are reached.

G. Levy [12] found the hypophysis normal in four instances where apparently there were no clinical signs suggestive of pituitary involvement.

Parhon, Ballif and Mârza [15] made a clinical and anatomical study of a case of post-encephalitic diabetes insipidus and infantilism. They attributed these conditions to changes in the hypothalamic region, and considered the hypophysis normal, but this seems questionable in view of their description. Urechia and Elekes [18] found changes in the tuber cinereum in three cases of epidemic encephalitis, but they do not give a detailed account of the hypophysis.

Stief [17], who mentions that anatomical findings in the hypothalamus have seldom been recorded, gives a short description of them in one case of epidemic encephalitis, and also describes various changes in the hypothalamic region in general paralysis and in arteriosclerotic disease.

On reviewing the work that has been done on the hypothalamic region in epidemic encephalitis, it is noteworthy that few workers have endeavoured to study a series of cases with a view to correlating the changes with clinical symptoms as has been done, for example, to a considerable extent in the case of the substantia nigra. It is easy to ascertain the degree of destruction in the latter structure owing to its compact form and the residual melanin pigment which is found even after the total disappearance of the cells. In the hypothalamic region owing to the more diffuse arrangement of some of the nerve-cells and the fact that there is not necessarily anything to mark the site of their disappearance, it is much more difficult to classify the changes as slight, moderate or severe, unless a number of brains are examined. We experienced this difficulty when we first began this investigation, and the final conclusions as to the significance of the alterations in the brain from a case of diabetes insipidus would have been quite different if this had been the only one examined.

THE HYPOTHALAMIC REGION OF THE BRAIN.

The nuclei of this region of the brain have been variously described by different authorities; and in lower animals, such as the dog, they do not always correspond with those in the human brain. We have followed the nomenclature of Foix and Nicolesco [7]. Figure 1, which is an outline of an actual section, gives an indication of the extent of the hypothalamic area examined in this investigation. The nuclei are represented diagrammatically.

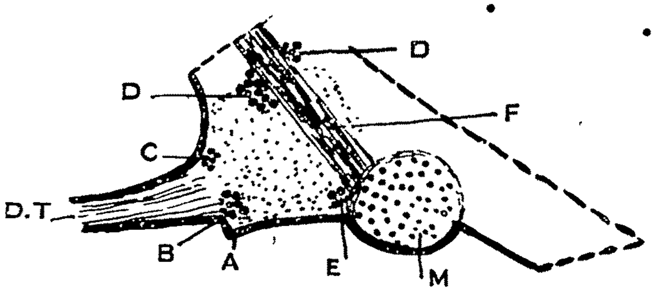

FIG. 1.—Hypothalamus. Outline of actual section (× 2½). Nuclei represented diagrammatically. O.T., Optic tract. A, Place of attachment of pituitary stalk. B, Ventral nucleus. C, Nucleus of the optic tract. D, Periventricular nucleus. E, Magnocellular nucleus. F, Anterior pillar of the trigone M, Corpus mammillare. The diffuse parvocellular nucleus extends over the whole infundibular region.

TEN CASES OF CHRONIC EPIDEMIC ENCEPHALITIS.

Nine cases were patients in the South Yorkshire Mental Hospital. In three (Cases 3, 5 and 9) the initial illness was slight or was not diagnosed until the development of Parkinsonism some time later. The duration of the disease in the ten cases varied from two to five years, Five of the ten patients died from the disease, two died from erysipelas of short duration, one from malaria used as an experimental therapeutic measure, one from chronic tuberculosis, and one from influenza and bronchopneumonia.

HISTOLOGICAL METHODS USED FOR THE EXAMINATION OF THE PITUITARY AND NERVOUS SYSTEM.

Pituitary.—After a preliminary short fixation in 10 per cent. formalin the pituitary was cut in half by an antero-posterior vertical section. A portion of the formalin fixed material was saved for frozen sections. The rest was fixed in Regaud's solution, and serial paraffin sections were made of it. The staining methods were as follows :—

(*a*) Weigert's iron hæmatoxylin and azo-eosin.

(*b*) Weigert's iron hæmatoxylin and Biebrich scarlet.

(*c*) Mallory's aniline-blue orange G with and without acid fuchsin. This method was useful owing to the difficulty of staining colloid and hyaline masses when present in the posterior lobe.

(*d*) A portion of the pituitary was embedded in gelatine and the formalized block cut frozen. The sections were examined for pigment and stained for fat with Scharlach R.

As it has been stated that post-mortem changes occur readily, we have examined several normal human and animal pituitaries, one piece being fixed immediately and other pieces fixed at varying intervals up to a period of forty-eight hours; we found only slight changes, no apparent alteration taking place in twenty-four hours, but in forty-eight hours slight vacuolation of some of the cells was discernible.

The nervous system.—Nearly all parts of the nervous system have been examined but are not here described in detail. Fixation was carried out in 10 per cent. formalin, and sections were mordanted in potassium bichromate when necessary.

The hypothalamic region.—Usually half was embedded in paraffin and the other half in celloidin, vertical sagittal sections being made and cut serially as far as possible.

For paraffin sections the methods used were:—

(*a*) Polychrome methylene-blue and alcoholic eosin.

(*b*) Methylene-blue and carbol-fuchsin, the latter being useful for the demonstration of increased pigment.

(*c*) Mallory's aniline-blue orange G with and without acid fuchsin.

For the celloidin sections the methods used were:—

(*d*) Weigert-Pal preparations, sometimes counterstained with alum carmine.

(*e*) Mallory's phosphotungstic acid and hæmatoxylin followed by differentiation in a 30 per cent. solution of ferric chloride.

(*f*) Frozen sections were sometimes used for the demonstration of neuroglia, the method being methyl violet preceded by Anderson's mordant.

In the description of the nervous system other than the hypothalamic region, emphasis is laid more especially on the condition of the cells of the substantia nigra, for as the degree of destruction of this area is readily ascertainable, it affords some standard of comparison.

CASE 1.—POST-ENCEPHALITIC DIABETES INSIPIDUS WITH OBESITY.

This case has been previously described in an account of diabetes insipidus (see p. 47).

CASE 2.—EARLY TRANSIENT NARCOLEPSY AND LATE CACHEXIA.

G. E. R., a man, aged 50 at death, had epidemic encephalitis in March, 1924, his first symptom being diplopia. He used to fall asleep suddenly in the street, and for this came into contact with the police. He became very depressed and was admitted to the South Yorkshire Mental Hospital in January, 1925. He then complained constantly of headache, of feeling cold of obscure abdominal sensations and of inability to sleep. In June, 1925, he had two epileptic fits, but none were noted afterwards. In December, 1925, he was in a typical Parkinsonian state. His intelligence remained good, but he continued to sleep badly and lost weight (about 2 st. in 1926). His urine contained no abnormal constituents, its specific gravity was 1015 in January, 1925, and 1020 in March, 1927. His general condition deteriorated and he finally died from the disease in December, 1927.

The pituitary seemed rather small. The pars anterior was congested and there was vacuolation of the cells, and in some of them there was a clear ring round the nucleus, particularly in the acidophiles.

Neither the pars intermedia nor pars nervosa showed unusual features except that in the latter there was a greater amount of pigment than normally. The small portion of the pars tuberalis around the stalk seemed normal. There were no globules of fat in any part of the pituitary.

The nervous system.—The brain weighed 46 oz. and there was perhaps some general wasting. This certainly was so in the hypothalamic region, and the brain-stem seemed unusually small. The third and one lateral ventricle were dilated.

There was no obvious tract degeneration apparent in Weigert-Pal preparations.

The mid-brain.—There was great destruction of nerve-cells, especially in the substantia nigra in which there was practically total disappearance of nerve-cells and increase of neuroglia. Around most of the blood-vessels there were numbers of small round cells, producing a cuffing which is more common in acute than chronic epidemic encephalitis.

The hypothalamic region.—In the corpus mammillare the nerve-cells exhibited chromatolysis. Many were vacuolated and contained pigment, but on the whole this structure was less affected than the other nuclei of this region. The cells of the magnocellular nucleus seemed to be fewer in number than normal, those remaining being in process of destruction, and the same was true of the periventricular nucleus. In the ventral nucleus of the tuber and the nucleus of the optic tracts, the changes were more intense and these nuclei could only be identified with difficulty as most of the cells had lost the greater part of their cytoplasm. Several hæmorrhages were found in the hypothalamic region, but these were not common elsewhere.

CASE 3.—PATHOLOGICAL DROWSINESS AND CACHEXIA.

M. M., a woman, aged 53 at death, was admitted in March, 1926, to the South Yorkshire Mental Hospital, the diagnosis being melancholia. She complained of depression and of inability to sleep owing to this. She had had influenza in 1924, and another severe attack just before admission. She stated later that on the second attack she had double vision. Epidemic encephalitis was not suspected at first. The only neurological sign present on the patient's admission to hospital was inequality and sluggish reactions of the pupils. The Wasserman reaction was negative. She complained at intervals of unusual feelings in the limbs. By December, 1926, she had become definitely Parkinsonian. She became progressively worse. From the beginning of 1928, she seemed to sleep all the time; she could be roused to answer questions, but immediately afterwards fell asleep again. A kyphosis developed and trophic changes were present. Her urine was normal. She became very emaciated, and died in September, 1928.

The exact amount of weight lost is not known, but she weighed only 5 st. 11 lb. a few months before death.

The pituitary.—The pars anterior was congested and immediately underneath the capsule were two hæmorrhages which extended into its substance, destroying two small areas. In the centre of the hæmorrhage isolated disintegrating cells could be seen. The pars anterior of this pituitary was more damaged than any other in the series. Most of the cells had either lost their cytoplasm or were very vacuolated (fig. 4.) Some of the remaining acidophiles had a swollen appearance. There were small areas with numerous nuclei but with the cytoplasm of the cells destroyed. This was probably originally an attempt at repair. Vesicles containing colloid and resembling the thyroid were common in the pars anterior. The cells in the portion of the pars tuberalis around the stalk were very vacuolated and many had lost all their cytoplasm.

There was a moderate amount of colloid in the pars intermedia, the cells of which invaded the pars nervosa, which was very congested. No fat globules stained by Scharlach R. in the pituitary, but fine pigment granules with some affinity for this dye were observed in the cells of the pars anterior.

The nervous system.—The brain weighed 44 oz. Some wasting was apparent in the hypothalamic region and in the right post-central area of the cerebral cortex. The brain was rather chocolate coloured and seemed firmer than normal. The Sylvian aqueduct and third ventricle were slightly dilated.

There were extensive changes throughout the whole nervous system, greater than in any other brain in this series. These changes were at a maximum in the mid-brain and hypothalamic region.

The nervous system stained fairly well by the Weigert-Pal method, but there was some tract degeneration in the lateral columns of the spinal cord and in the medulla.

The mid-brain.—The cells of the substantia nigra had disappeared as in Case 2. Many fibres were obviously abnormal, as they presented varicosities and constrictions, the appearance being similar to the "beaded" effect observed by McAlpine in the substantia nigra in other cases. This was present in other parts of the nervous system but to a much less extent, except in the hypothalamic region where it was also a characteristic feature.

The hypothalamic region.—The cells of the corpus mamillare were diminished in number, contained no Nissl granules, and many were completely filled with pigment. The cells of the magnocellular nucleus were swollen and stained a dull red in methylene-blue and eosin preparations. In the part of the periventricular nucleus posterior to the anterior pillar of the trigone there was a hæmorrhage, and only a few cells remained. In the anterior part of this nucleus all the cells were abnormal, being either filled with pigment or staining abnormally. In the ventral nucleus of the tuber the destructive changes were still greater, and there was an old hæmorrhage about the site of the nucleus of the optic tract.

The increase of neuroglial cells and fibres was not sufficient to compensate for the destructive processes, as this area showed the condition "status spongiosus," described by Spielmeyer in other conditions, in different parts of the nervous system (fig. 7). There was practically no cuffing of the blood-vessels, but occasionally there were cells outside the vessels, more commonly plasma than round cells. Hæmorrhages were very numerous; in the hypothalamic region, in addition to those already mentioned, there were several other old and recent ones (fig. 6). The age of the hæmorrhage was indicated to some extent by the amount of increase of neuroglia around it, and also by disintegrating masses of pigment. Similar hæmorrhages were present in the mid-brain, in the nuclei of the ninth and tenth nerves, and in the spinal cord.

CASE 4.—POST-ENCEPHALITIC MANIA, EPILEPTIFORM ATTACKS AND SUDDEN DEATH.

D. F. B., a girl, aged 18 at death, had epidemic encephalitis in March, 1924, when she had diplopia, occupation delirium, and drowsiness. She complained later of insomnia, but on the whole she remained drowsy. By May, 1926, she had become slower in her movements, rigidity was present on the right side and myotonia in the right hand. She began to have "dizzy" bouts, in which she would fall. In September, 1926, tremors were troublesome, and she usually then slept heavily in the morning. By August, 1927, she was occasionally excitable and had epileptiform attacks. After an attempt at suicide prompted by auditory hallucinations she was admitted to the South Yorkshire Mental Hospital in October, 1927. She became impulsive and dangerous. In April, 1928, she was placed one day in a side room owing to previous excitement, and she was found dead an hour later.

There was no noticeable alteration in weight during the patient's stay in the South Yorkshire Mental Hospital.

The pituitary was of average size (0·6 grm.). It was very congested. In the pars anterior there were two or three irregular-shaped masses of colloid material containing remains of cells, but the majority of the cells were well formed and the relative number of chromophile cells was within normal limits. There was a slight increase of connective tissue. The cleft between the lobes was unusually patent and contained a small amount of colloid material. The posterior lobe showed nothing unusual. There was no fat stainable by Scharlach R. in any part of the pituitary.

The nervous system.—The brain weighed 43 oz. and there was no wasting.

It was very congested, but compared to some of the other brains in the series the histological changes in many areas were comparatively slight. There was no obvious tract degeneration in Weigert-Pal preparations.

The mid-brain.—In the substantia nigra the nerve-cells were very little altered compared to the rest of the series except those in Case 1, and no difference was observed in the cells of the two sides (rigidity had existed mainly on one side).

In the hypothalamic region the alterations in the nerve-cells were less than in Cases 2 and 3. The cells contained an unusual amount of pigment considering the age of the patient, and there was a spongy condition in some areas, as in Case 3. This was not due to the fixation, which was good in the rest of the nervous system. The corpus mammillare showed only comparatively slight alterations except that a small mass of pigment in its posterior part indicated an old hæmorrhage. Some of the cells of the magnocellular nucleus and many of the periventricular nucleus were intact. In the anterior part of the latter structure there was a small hæmorrhage and a large one immediately anterior (fig. 7). In the ventral nucleus many cells were vacuolated, but there was less alteration than in the nucleus of the optic tracts. Multiple hæmorrhages were a characteristic feature in both the hypothalamic region and mid-brain, though none were observed in the cerebral cortex nor in the pons and medulla.

Calcium content.—Although the cerebral cortex was comparatively normal histologically, there were noteworthy alterations in its calcium content. This amounted to 9·5 mg. calcium in 100 grm. of cortex as compared to an average of 4 to 4·5 mg. at this age. As far as could be judged from histological appearances there was even greater increase of calcium salts in the hypothalamic region.

No changes were found in other organs of the body.

CASE 5.—CACHEXIA.

W. B., a man, aged 52, was admitted to the South Yorkshire Mental Hospital about two years before death, with a provisional diagnosis of confusional insanity. Some months later he was noticed to be apathetic and drowsy and began to develop Parkinsonism. A diagnosis of epidemic encephalitis was then made. The Parkinsonian condition was extreme and the patient was wasted at the time of his death from this disease, about eighteen months later.

The pituitary.—This weighed 0·7 grm.—slightly greater than the normal weight. Some congestion was present. In the pars anterior the majority of the cells were acidophiles, small in size and with darkly staining nuclei. The cells were not otherwise abnormal. There appeared to be hyperplasia, particularly of the pars anterior (fig. 3) but also to a slight extent in the pars intermedia, in which there was an average amount of colloid arranged in vesicles. The pars nervosa showed nothing unusual.

The nervous system.—The brain weighed 45 oz. A description of the nervous system, with the exception of the hypothalamic region, which unfortunately was not available for examination, has been already published [5].

CASE 6.—NO ALTERATION IN WEIGHT.

A. N., a man, aged 28 at death, had epidemic encephalitis in May, 1924. After an attempt at suicide he was admitted to the South Yorkshire Mental Hospital in September, 1925. He was then very depressed, complained of not sleeping at night and of pains in his arms. He was in an advanced Parkinsonian state. He constantly complained of pains in the arms and shoulders. In September, 1927, he developed erysipelas and died seven days later.

In September, 1925, his weight was 10 st. 6 lb. (height 6 ft.), and in September, 1927, 10 st. 9 lb. There was no abnormality in the urine, the specific gravity of which was 1022.

The pituitary.—The pars anterior was congested, especially the vessels at the junction of the two lobes. The cells were mainly acidophiles and slight hyperplasia was present. The pars intermedia and pars nervosa appeared normal except for some increase of connective tissue at the junction.

The nervous system.—The weight of the brain was not known, but it seemed unusually small. There were changes throughout the nervous system, most marked in the mid-brain. Some degeneration of the lateral columns of the medulla was apparent in Weigert-Pal preparations.

The mid-brain.—The walls of the blood-vessels were thickened. In the substantia nigra there was considerable destruction of nerve-cells.

The hypothalamic region.—There were pathological changes in the nerve-cells, but the appearances in the different nuclei are not described, as such lesions may be brought about by a high temperature. In Weigert-Pal preparations the nerve-fibres were altered and, as in Case 3, presented a beaded appearance, and there was increase of neuroglial fibres in the tuber cinereum. The latter changes must be attributed to epidemic encephalitis.

CASE 7.—POST-ENCEPHALITIC OBESITY.

G. F. G., a man, aged 31 at death, had an attack of "influenza" in December, 1925, and had double vision occasionally. He became very depressed and on admission to the South Yorkshire Mental Hospital in July, 1926, he was in a Parkinsonian state and unable to walk. He had occasional epileptic fits, but had been subject to epilepsy since the age of 19.

His weight increased progressively from 7 st. 8 lb. in July, 1926, to 10 st. 7 lb. in September, 1927.

He died in February, 1928, two days after contracting erysipelas.

The pituitary.—A large amount of colloid could be seen between the anterior and posterior lobes. The pituitary was of rather unusual form, being elongated in an antero-posterior direction. The anterior lobe was congested, a fair number of acidophiles was present, but the cells were unusually discrete. The large mass of colloid showed variations in its staining properties in different areas. At the junction of the pars intermedia and pars nervosa and in the latter, was a group of cells rather similar to mucous acini. Possibly these had nothing to do with the encephalitic condition, as a similar appearance has been seen by the writers in the case of another epileptic. The fibres of the pars nervosa were unusually widely separated.

The nervous system.—The brain weighed 49 oz. and there was no apparent wasting.

The mid-brain.—The substantia nigra was very severely damaged, most of its cells being destroyed.

The hypothalamic region.—Although all the nerve-cells were more or less abnormal, there was less destruction than in some of the cases (e.g., 2 and 3) ; the different nuclei could be recognized, but as all were affected it is difficult to make comparisons.

In the corpus mammillare the number of nerve-cells appeared fewer and more abnormal than in Case 1. The magnocellular and periventricular nuclei were comparatively little altered. In the ventral nucleus of the tuber there were fewer cells than normal. There were two small hæmorrhages in the hypothalamic region, probably of recent origin. One was immediately anterior to the corpus mammillare.

CASE 8.

G. F. H., a man, aged 32 at death, had epidemic encephalitis in December, 1924. He became very depressed and was admitted to the South Yorkshire Mental Hospital in July, 1926. He was then in an advanced Parkinsonian condition. There had been very little alteration in weight. In November, 1927, he was inoculated with malaria as a therapeutic measure. Rigors took place each day from November 21 till 27, when he collapsed and died.

The pituitary.—The pars anterior was congested and there was total destruction of the cytoplasm of many of the cells and dissociation of practically all (fig. 5.) The destructive changes were greater in this than in any other in the series except No. 3.

The nervous system.—The brain weighed 50 oz.

Mid-brain.—The cells of the substantia nigra were almost completely destroyed.

In the hypothalamic region there were considerable destructive changes, but a detailed account of the different nuclei is not given as the high temperature due to malaria could be regarded as a sufficient cause for changes in nerve-cells.

CASE 9.

A. H., a woman, aged 34 at death, had an attack of " influenza " in February, 1924. She became very depressed and obsessed with different ailments which were regarded at the time as imaginary. She attempted suicide and was admitted to the South Yorkshire Mental Hospital in May, 1924. There were then no neurological signs. In March, 1925, she was found to have phthisis. Early in April, 1928, Parkinsonism, which was considered to be post-encephalitic, was apparent. She also developed a left hemiplegia, the leg being more affected than the arm. The specific gravity of the urine was 1016 and albumin was present. She died in January, 1929, from tuberculosis and chronic epidemic encephalitis.

The pituitary.—The pituitary weighed 0·9 grm. and was heavier than any other in the series. There was a considerable amount of destruction of the cytoplasm of the cells of the pars anterior, and a fair amount of colloid between the two lobes.

The nervous system.—The brain weighed 44 oz. It was very pale and there seemed to be slight wasting, particularly on the right side. In Weigert-Pal preparations there was some degeneration of one pyramidal tract.

Mid-brain.—There was destruction of nerve-cells with separation of pigment in the substantia nigra.

Hypothalamic region.—There were destructive changes in the different collections of nerve-cells.

CASE 10.

A. E. S., a woman, aged 62 at death, had epidemic encephalitis in March, 1924. She was admitted to the South Yorkshire Mental Hospital in October, 1926, and was then very depressed and complained constantly of inability to sleep. She was very Parkinsonian. She did not improve, but did not lose weight. There was no abnormality in the urine. She had an attack of influenza in March, 1929, and died from this after a short illness.

The pituitary.—This weighed 0·85 grm., a greater weight than any in the series except No. 8. There was great congestion in the anterior lobe. A fair proportion of eosinophiles was present, many of which were vacuolated. Nearly all the cells were unusually discrete; in some the cytoplasm was destroyed. In the posterior lobe the most noteworthy feature was some hyperplasia of the pars intermedia. Possibly there had been originally hyperplasia of the anterior lobe and later slight destructive changes.

The nervous system.—The brain weighed 43 oz. The right lateral ventricle was slightly larger than the left.

The nerve-cells throughout the whole nervous system were damaged, but most severely in the hypothalamic region and mid-brain.

The mid-brain.—There were severe destructive changes in the substantia nigra.

The hypothalamic region.—Status spongiosus was present. In the meninges of the hypothalamic region there was a collection of small round cells which extended into the brain substance (fig. 8); this may have been a terminal infection.

SUMMARY OF APPEARANCES IN PITUITARY AND HYPOTHALAMIC REGION AND OF SOME CLINICAL SYMPTOMS.

Case and duration of disease	Remarks	Pituitary			General remarks on nervous system	Hypothalamic region	Substantia nigra (and a note on Parkinsonism)
		Pars anterior	Pars intermedia	Pars nervosa			
I. — W. L., 2 yrs. 4 mths.	Diabetes insipidus. Obesity. Epilepsy	Hyperplasia in some areas	Hyperplasia. Increased connective tissue bounding islands of cells. Large amount of colloid in vesicles and cysts	More colloid and hyaline masses than usually seen. Moderate amount of pigment	No wasting of brain	Less destructive changes than any in series. All nuclei affected, but no comparison possible	Slight changes. (Never more than a slight suspicion of Parkinsonism)
II.—G. E. R., 3 yrs. 8 mths.	Cachexia. Originally narcoleptic attacks. Later insomnia	Slight vacuolation of some cells. Decrease in size of pituitary	No conspicuous abnormality	Pigment ..	Some wasting, especially in hypothalamic region. The third and one lateral ventricle dilated	Severe destructive changes, probably the most marked in the ventral nucleus	Severe changes. (Advanced Parkinsonism)
III. — M. M., 2 yrs. 6 mths.	Cachexia. Extreme drowsiness for many months	Very abnormal. Total destruction of cytoplasm of most cells. Two hæmorrhages	No conspicuous abnormality	Pigment ..	Wasting in hypothalamic region and in right post-central area. The Sylvian aqueduct and third ventricle slightly dilated. Multiple hæmorrhages in brain-stem and hypothalamic region	Status spongiosus. All nuclei affected. Multiple hæmorrhages a characteristic feature	Severe changes. (Very advanced Parkinsonism)
IV.—D. F. B., 4 yrs.	No noticeable alteration in weight. Epilepsy	Not particularly abnormal	No conspicuous abnormality	No conspicuous abnormality	No wasting of brain. Multiple hæmorrhages in hypothalamic region and mid-brain	Changes in nerve-cells, but less than in other cases, except I and VII. Multiple hæmorrhages a very characteristic feature	Changes comparatively slight. No difference in cells of two sides. (Rigidity mainly on one side)

V.—W. B., more than 2 yrs.	Cachexia. Drowsiness many months after onset of disease	Hyperplasia ..	Slight hyperplasia	No conspicuous abnormality	Brain weight rather low	Not available for examination	Severe changes (Advanced Parkinsonism)
VI. — A. N., 3 yrs. 11 mths	No noticeable alteration in weight. Insomnia	Slight hyperplasia	Slight increase of connective tissue at the junction of the intermedia and nervosa	No conspicuous abnormality	Brain unusually small	Severe destructive changes	Severe changes. (Advanced Parkinsonism)
VII.—G. F. G., 2 yrs. 2 mths.	Obesity. Epileptic before the onset of encephalitis	Cells unusually discrete	Large mass of colloid between the two lobes	Group of cells similar to mucous acini at junction of pars intermedia and nervosa	No wasting of brain	Less destructive changes than in the others, except I and IV. Corpus mamillare more abnormal than that of Case I	Very severe changes. (Very advanced Parkinsonism)
VIII.—G. F. H., 2 yrs. 6 mths.	Treated by malaria. No alteration in weight	Very abnormal. Dissociation of cells	No conspicuous abnormality	No conspicuous abnormality	No wasting of brain	Severe destructive changes	Severe changes. (Parkinsonism)
IX. — A. H., 5 yrs.	Cachexia, but patient had phthisis 4 yrs.	Abnormal. Destruction of cytoplasm	No conspicuous abnormality	No conspicuous abnormality	Slight wasting on right side of brain	Severe destructive changes	Severe changes. (Very advanced Parkinsonism)
X. — A. E. S., 5 yrs.	Weight well maintained. Insomnia	Originally hyperplasia followed by slight destructive changes	Hyperplasia ..	No conspicuous abnormality	Brain weight low. Right lateral ventricle slightly larger than left	Status spongiosus. Infiltration of meninges with small round cells	Severe changes. (Advanced Parkinsonism)

DISCUSSION OF THE APPEARANCES IN THE PITUITARY.

It will be seen that in chronic epidemic encephalitis, although the pars anterior is sometimes normal, it may be either hyperplastic or atrophic, and the pars intermedia may also be hyperplastic. We may suppose that whereas the pituitary may react by hyperplasia, the virus of epidemic encephalitis ultimately produces secondary atrophic changes.

It is necessary to consider in the five cases that died from causes other than epidemic encephalitis how far the pathological changes may be ascribed to other diseases. Of the two patients with erysipelas, in one the pituitary was not very abnormal and in the other the disease was probably of too short duration to have had any influence.

Case 8 died from malaria, and the pars anterior is in many respects more abnormal than any of the others except that in Case 3, and in all probability this was due to malarial infection. We have not found any description in the literature of the pituitary in malaria, but there is a scarcity of information in general about the effect of different diseases on the pituitary.

Case 9 died from tuberculosis and the pituitary was heavier than any in the series, a feature common in this disease. No stress can therefore be laid on the appearances seen in the pituitary.

DISCUSSION OF POSSIBLE RELATIONSHIP TO SYMPTOMS OF CHANGES IN THE PITUITARY AND HYPOTHALAMIC REGION.

Diabetes insipidus.—The relation of lesions in the pituitary to diabetes insipidus has been already discussed by one of us (see p. 47). The important fact which emerges from a comparative study of the hypothalamic region in the ten cases is that diabetes insipidus does not occur when the changes in this area are very severe, although it may do so when they are less intense.

Obesity.—That there is an anti-diuretic hormone produced by the pituitary, a deficiency of which causes diabetes insipidus, seems to us to be proved. There is as yet no equally good evidence of the importance of a pituitary hormone in relationship to obesity. The supporters of the possible hypophyseal origin of obesity regard the condition as due to a deficiency of hormone, but there is a difference of opinion as to which lobe of the pituitary is affected. If the posterior lobe is responsible, it is difficult to understand why obesity is not more commonly associated with diabetes insipidus. It may, however, be pointed out that in both the cases with obesity there was an unusual increase of colloid in the posterior lobe, which may be regarded as a possible stasis of secretion. Otherwise, we find it difficult to express an opinion. In neither case was the anterior lobe particularly abnormal.

In all the ten cases of encephalitis there were alterations in the hypothalamic region. The changes were rather less advanced in the cases in which obesity existed. This corresponds with clinical observations that post-encephalitic obesity—where it occurs—is usually an early sequel. A. J. Hall and A. G. Yates [10] refer to the rapid increase in weight in some of their cases a few months after the primary attack of encephalitis, and state that this occurs before the recognized onset of Parkinsonism. According to Stern [16] also, obesity is usually an early symptom, but instances have been recorded of the appearance of obesity as long as four years after the acute stage. In Case 1 in this paper obesity was first noticeable about eighteen months after the acute attack, and polyuria appeared about the same time. In Case 7 a definite increase in weight took place about a year after the acute attack, and a severe degree of Parkinsonism was then present. Post-encephalitic obesity may be transient and followed by cachexia. On the other hand, it may persist until the death of the patient from the disease, or it may disappear with recovery of the patient from encephalitis. Whatever the mechanism of production of obesity, the exciting cause seems to be a mild rather than a severe lesion. Isolated examples of obesity and very severe destructive lesions in the hypothalamic region do not disprove this, as obviously this condition, unlike diabetes insipidus, when once produced, cannot disappear instantaneously.

Cachexia.—The relationship of destructive changes in the pars anterior to the presence of cachexia in epidemic encephalitis is doubtful as it is obviously debatable as to which is cause and which is effect. In Case 3 the patient was very emaciated, and destructive changes in the pars anterior were at a maximum. However, Case 5 lost weight considerably, and the pars anterior was hyperplastic. It therefore seems the more probable that cachexia in epidemic encephalitis is independent of any changes in the pituitary.

In the nine cases where the hypothalamic region was examined, severe pathological changes were found in this area in seven, although cachexia occurred in two only of them. We therefore hesitate to conclude that such changes are the cause of the condition, although it must be admitted that some time must elapse for cachexia to be established if destructive changes in the nervous system are a cause.

There is a type of Parkinsonism accompanied by severe wasting.

That there is necessarily a common cause for the two conditions seems, however, to be disproved by such a case as No. 7 in our series. This patient began to gain in weight after severe Parkinsonism was established; the destructive changes in the substantia nigra were severe, those in the hypothalamic region comparatively slight.

Disorders of sleep.—The pathology of disturbances of sleep is uncertain, although it has been much discussed. Various theories about the nature of sleep are discussed, and there is reference to much of the literature in papers by Adie [1], Fulton and Bailey [6] and Kinnier Wilson [19]. The latter author remarks on the incomplete nature of pathological knowledge on the subject of sleep disorders. It has been suggested that the pathological drowsiness of epidemic encephalitis may be of pituitary origin. However, Cases 5 and 6 suffered from sleep disturbances and the pituitary in both instances was very slightly abnormal, so it seems improbable that abnormalities in the pituitary in the other cases played a part in the causation of these symptoms.

In a disease such as epidemic encephalitis which attacks the nervous system diffusely the problem is obviously a difficult one. As is well known, the disturbances of sleep are of four kinds: (*a*) hypersomnia; (*b*) insomnia; (*c*) reversal of the sleep rhythm, and (*d*) narcolepsy, and which type predominates may vary in the same patient at different stages of the malady. Case 2, for instance, at an early stage had narcoleptic attacks and later complained of insomnia. Case 3 originally suffered from insomnia, and two years later from hypersomnia.

Hypersomnia, or excessive sleepiness, is found as a symptom in several conditions, cerebral tumours being perhaps the commonest apart from epidemic encephalitis. Statements vary as to the frequency of its occurrence in tumours in different parts of the brain, but it is probably most common in tumours in the neighbourhood of the hypothalamus and pituitary.

It will be seen that the hypothalamic region was affected in all the ten cases of the series, but it does not, of course, necessarily follow that it was responsible for all the sleep disturbances. Cases 2 and 6, for example, frequently complained of spontaneous pains in the limbs, and this might be sufficient to account for insomnia. The existence of old hæmorrhages in the hypothalamic region in Case 3 is interesting in view of the onset of extreme drowsiness about ten months before death.

A point of great importance which has been little considered is the frequency of changes in the hypothalamic region without disturbance of sleep. Stief [17] described various changes in the hypothalamic region in general paralysis and in arterio-sclerotic disease. Yet there is no mention of these patients having had disorders of sleep. An examination of the photomicrographs in Stief's paper inclined us to the opinion that the cell destruction was small and the increase of neuroglia very great as compared with these cases of chronic epidemic encephalitis. We have, however, felt it advisable to examine the hypothalamic region from cases in which there was extensive degeneration of the nervous system in order to make a more certain comparison. We selected brains from cases of Huntington's chorea and general paralysis of the insane for this purpose. In the hypothalamic region from the case of Huntington's chorea the different collections of nuclei could easily be identified and there was very little destruction of nerve-cells. The same was true in the hypothalamic region from a case of general paralysis of the insane with the difference that there was considerable increase of neuroglial nuclei.

There is another point of view that seems worth mentioning. Perhaps there is a not unnatural tendency to overstress the histological appearances without considering biochemical differences that may exist in different conditions, but, indeed, little work has been done in this direction.

One of us has found by chemical analysis of the nervous system that a raised calcium content is relatively common in epidemic encephalitis, but is rarely found in general paralysis of the insane. Why one nervous disease should be accompanied by increased calcium, and why this should not be so in a severe degenerative condition such as general paralysis of the insane, seems rather mysterious, but in view of Demole's work it may have some bearing on disorders of sleep. Demole's experiments resulted from the observations of Cloetta and Thomann that the amount of calcium in the blood falls during sleep, a possibility being that it is concentrated in the brain. Demole [4] found that by injecting weak solutions of calcium salts into the region of the floor of the third ventricle, sleep could be induced in animals, and that an antagonistic effect was produced by potassium salts. The specific action of these salts was confined to the hypothalamic region.

These striking experiments have been repeated by Marinesco, Sager and Kreindler [14], who confirmed the observation that calcium injections into the hypothalamic region favoured sleep. These workers were also able to produce reversible sleep phenomena in animals.

SUMMARY.

(1) In chronic epidemic encephalitis there is frequently some change in the pituitary.

(2) The hypothalamic region of the brain in chronic epidemic encephalitis is more severely affected than any other area except the substantia nigra of the mid-brain. The changes in the two regions are usually, but not invariably, parallel.

(3) In all the cases of epidemic encephalitis the changes in the hypothalamic region were greater than in the same area in brains from cases of Huntington's chorea and general paralysis of the insane, where elsewhere there were severe degenerative changes.

(4) Severe lesions in the hypothalamic region do not give rise to diabetes insipidus nor to obesity, but less intense lesions may cause these conditions.

The part played by the pituitary in the production of obesity remains uncertain.

(5) Cachexia is probably independent of any changes in the pituitary. There is no absolute proof, although there is a possibility, that pathological alterations in the hypothalamic region are the cause of cachexia. On the other hand, it seems certain there is no causal relationship between destruction of the substantia nigra and cachexia.

(6) There is not any definite relationship between disturbances of sleep in epidemic encephalitis and alterations in the anterior lobe of the hypophysis. As the hypothalamus was affected in all the brains, and is not commonly the chief site of attack in other degenerative diseases, disturbance of its function—perhaps due to increase of calcium salts—probably plays some share in the causation of disorders of sleep. An increase of calcium salts does not usually occur in conditions such as Huntington's chorea and general paralysis of the insane.

(7) Hæmorrhages were more common in the hypothalamic region and mid-brain than elsewhere, and may have been the cause of sudden death in one young patient.

The writers are very much indebted to Professor Hall for some helpful criticism and advice. They wish to thank the Medical Superintendent and the Senior Medical Officers of the South Yorkshire Mental Hospital for facilities for studying the cases on which this paper is based; Dr. Thorpe, the pathologist, for the supply of material; and Dr. Elizabeth Sykes for information about the weights of patients.

PLATE VIII.

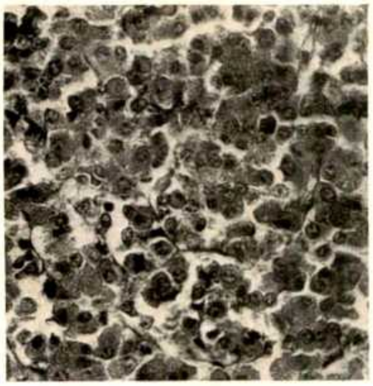

FIG. 2.

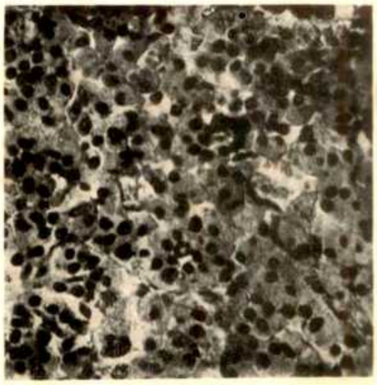

FIG. 3.

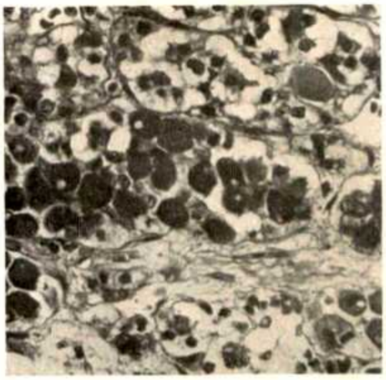

FIG. 4.

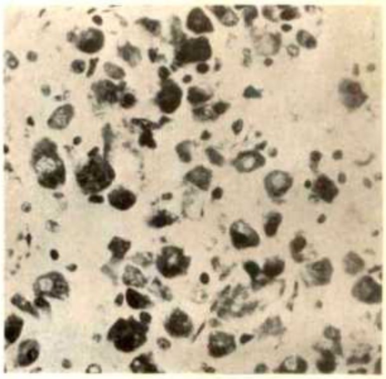

FIG. 5.

To illustrate article by Elizabeth Cowper Eaves and Margaret M. Croll.

PLATE IX.

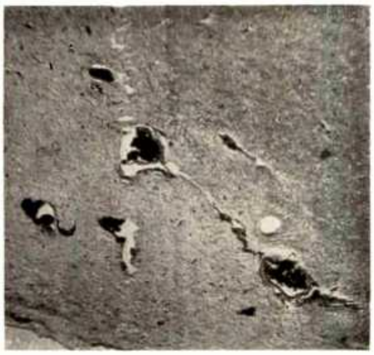

FIG. 6.

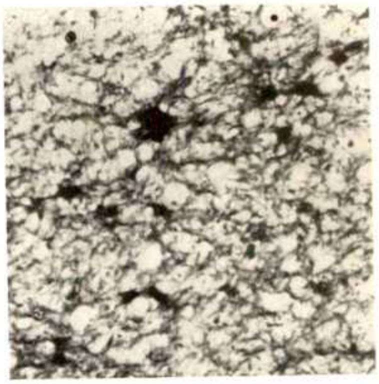

FIG. 7.

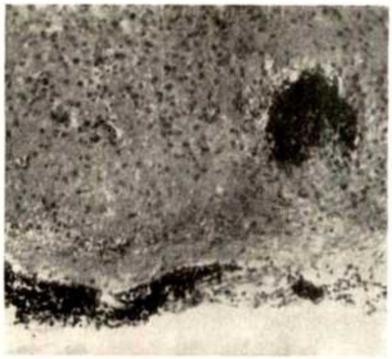

FIG. 8.

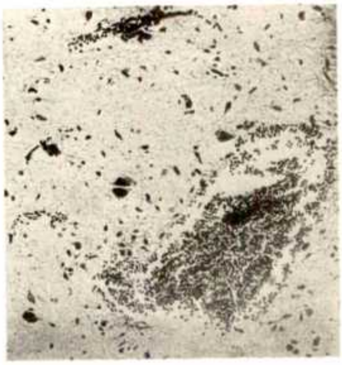

FIG. 9.

To illustrate article by Elizabeth Cowper Eaves and Margaret M. Croll.

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DESCRIPTION OF ILLUSTRATIONS, PLATES VIII AND IX.

FIG. 2.—Pars Anterior of the Pituitary. Originally × 500 reduced to ⅔. Normal for comparison with fig. 3.

FIG. 3.—Pars Anterior of the Pituitary. Originally × 500, reduced to ⅔. *Case* 5. Hyperplasia. The nuclei are more numerous and more darkly staining than those in the normal pars anterior in fig. 2. Some of the cells are binucleated.

FIG. 4.—Pars Anterior of the Pituitary. Originally × 500, reduced to ⅔. *Case* 3. Atrophy. Many of the cells have lost all the cytoplasm. About the centre of the field is a group of swollen eosinophiles.

FIG. 5.—Pars Anterior of the Pituitary. Originally × 500 reduced to ⅔. *Case* 8 (treated with malaria). Dissociation of cells which are practically all isolated and vacuolated.

FIG. 6.—Hypothalamic region. Originally × 40, reduced to ⅔. *Case* 3. Hæmorrhages—most of them not recent.

FIG. 7.—Hypothalamic region. Originally × 500, reduced to ⅔. *Case* 3. Status spongiosus.

FIG. 8.—Hypothalamic region. Originally × 140, reduced to ⅔. *Case* 4. Hæmorrhage.

FIG. 9.—Hypothalamic region. Originally × 140, reduced to ⅔. *Case* 10. Numerous round cells in the meninges, extending into the substance of the hypothalamic region.

EXPERIMENTAL DIABETES INSIPIDUS.

BY CURT P. RICHTER.

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THAT there is a close relationship between water exchange and the function of nervous tissue of the brain-stem surrounding the sella turcica has been indicated by a number of different observations, clinical and experimental. Tumours of this region are sometimes associated with either temporary or permanent polydipsia and polyuria or diabetes insipidus. Experimental lesions of this region, even very minute injuries, have been followed by increased water-intake and urine-output which lasted only a few hours or days, but in a few instances seemed to be permanent. Camus and Roussy (1922), and Bailey and Bremer (1921) in their experiments, each had one animal in which the diabetes insipidus seemed to be permanent. The production of permanent effects, however, is still entirely a matter of chance. Experimentally the problem is still incompletely solved. We do not know what structures are injured when the diabetes is produced, nor do we know how the lesion operates.

For the solution of this problem it is important to be able to produce a permanent effect consistently and under controlled conditions. The rat is a suitable animal for this purpose. It will be shown below that permanent polydipsia and polyuria may be produced in this animal very simply by means of brain-stem puncture, while the brain is large enough to permit definite localization of the injury to be made. In addition, the size of the rat allows it to be kept in a cage in which the water-intake, urine-output, and other changes can be accurately measured.

In the present paper the method of making the puncture is described, and records of the effects on water-intake and urine-output produced in this way are given. The results of the histological study of the brains of these animals will be described in a later paper.

METHODS.

The method of puncturing the brain (fig. 1) is the same as that used by Philip Smith (1927) in his operations on the pituitary body. The anæsthetized rat is tied on its back to a small board and the hair is enclosed by the dotted line in fig. 2 is stripped of adherent membranes and other tissues so that the median suture may be located. Then a stab is made directly through the bone with the scalpel shown in fig 2. The depth of the thrust is regulated by means of a drop of solder attached at the side of the scalpel to act as a stop. The bone is soft enough even in old animals to permit easy penetration of the scalpel. A sagittal view is shown in fig. 3.

Since the albino rat is strongly resistant to infection no antiseptic precautions are necessary for the operation. None of the thirty-six animals used in the present experiment became infected.

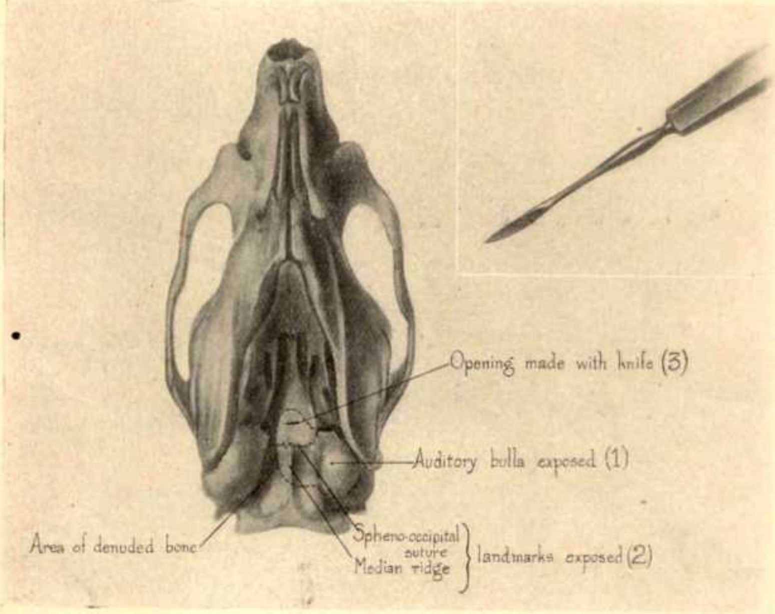

FIG. 2.—Drawing of the skull of the rat and the scalpel used in making brain-stem punctures.

The rats were kept separately in cages described in detail elsewhere (Richter and Wang, 1926) (Richter, 1927) in connection with studies on running activity. These cages consist of a small living compartment with easy access to a revolving drum in which the animal may run. The revolutions of the drum are recorded on a ratchet cyclometer. The cage contains, besides a space large enough for an adult rat to sleep in, a food-box and a graduated inverted watering-tube. Daily records were made of running activity and food and water-intake. The urine was collected from both the living compartment and the revolving drum by clipped away from the skin of the neck. A longitudinal incision about 1 cm. in length is then made to the right of the midline to expose the masseter muscle, as shown in the drawing in fig. 1. A blunt probe is inserted at the point indicated and pushed straight downwards until it reaches the auditory bulla which can be easily recognized by its spherical shape. A second probe is introduced beside the first and the two are spread apart in the longitudinal direction. In this way the muscles covering the auditory bulla may be separated without injuring the muscles themselves or the surrounding blood-vessels. The area of bone

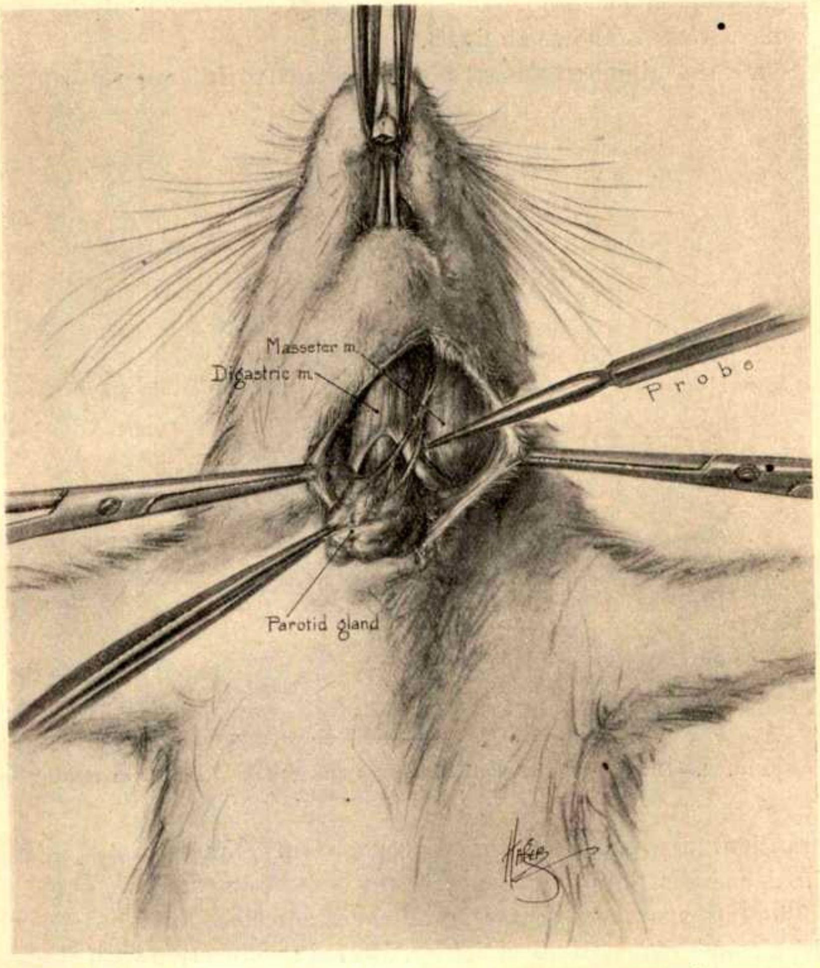

FIG. 1.—Drawing showing incision in rat's neck and opening between the masseter and diagastric muscles through which the base of the skull is exposed.

means of pans with funnel-shaped bottoms placed beneath the mesh-wire floor of the cages and leading into small graduated cylinders. The condition of the reproductive tract was studied by means of daily vaginal smears. And finally, the rate of growth was charted by weekly records of the body-weight.

Thirty-six female rats were used for the experiments, their ages at the time of the brain punctures varying from forty to one hundred and twenty days. Females were used exclusively because, by means of vaginal smears, changes in the function of the sex-glands can be most easily detected, and such changes are significant because they can be produced by injuries to the pituitary glands.

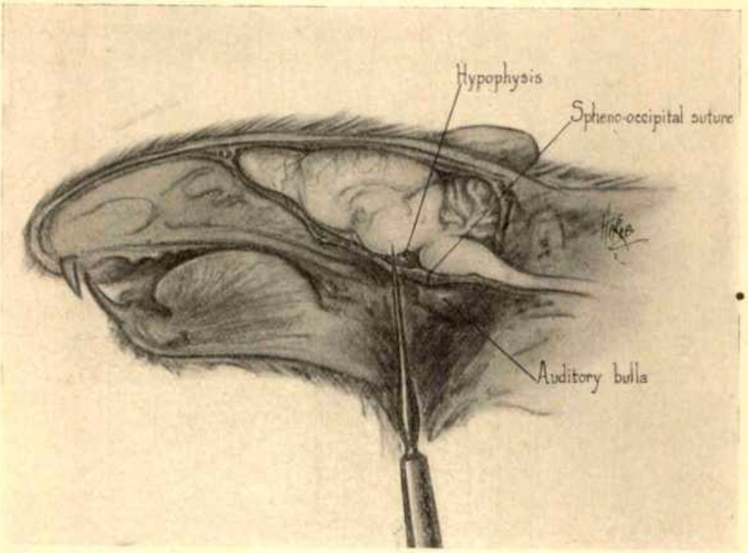

FIG. 3.—Sagittal section of the rat's head showing where the scalpel pierces the skull and brain.

RESULTS.

The brain-stem was punctured at different levels within a very limited region. This region can be located in the skull in fig. 2 with relation to the spheno-occipital suture. In the average adult rat it extends from 3 mm. above the suture to 0·5 mm. below. This part of the skull covers the pituitary gland and leaves a margin of approximately 0·5 mm. above and below.

Of the thirty-six animals used for these experiments seven showed

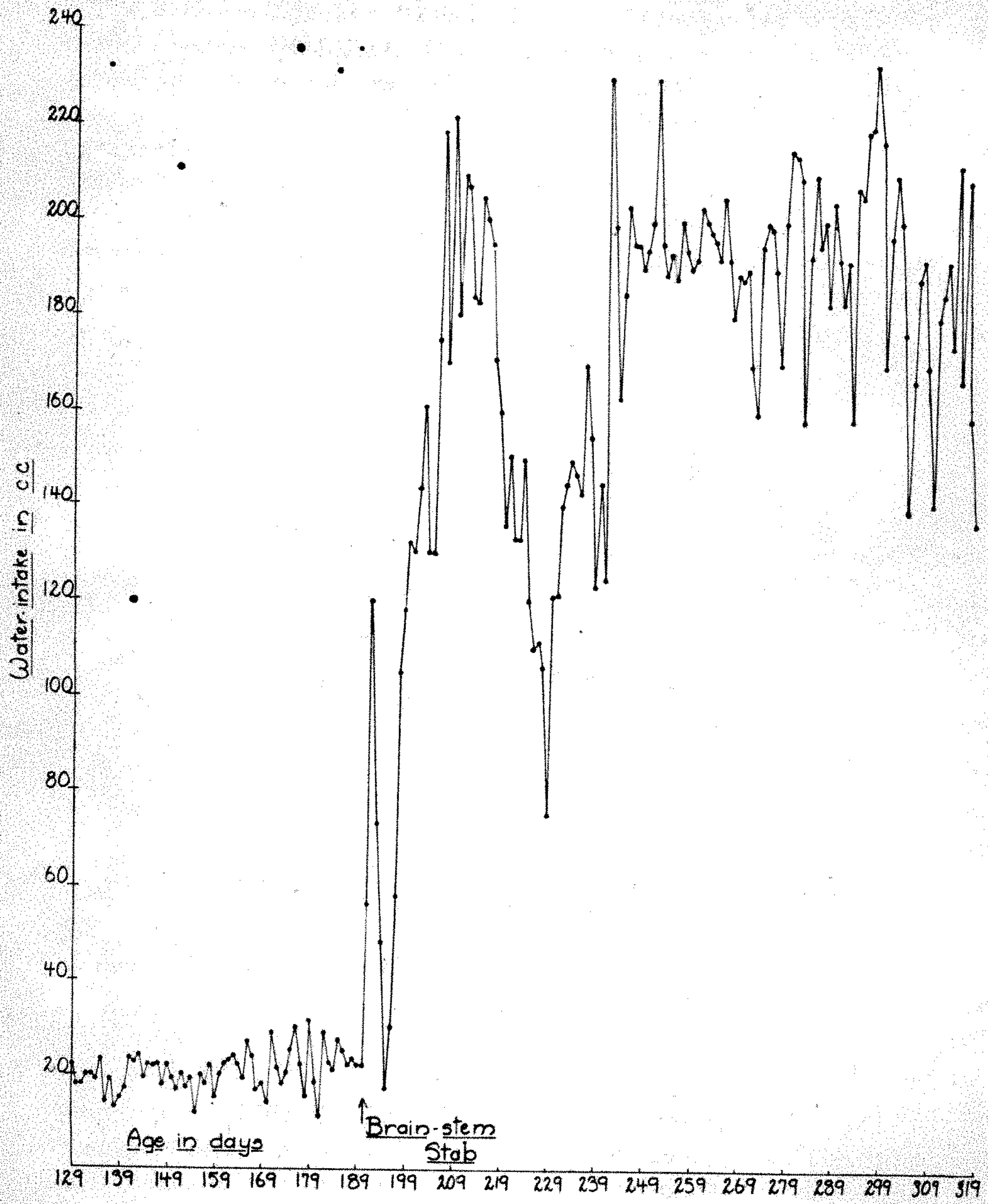

FIG. 4.—Water-intake record showing effect of brain-stem puncture. The ordinates give water-intake in cubic centimetres and the abscissæ the duration of the experiment in days. Rat 430.

an increase in water-intake as a result of the puncture. Post-mortem examination showed that the scalpel penetrated the skull in all seven at the same level, 2·5 to 3 mm. anterior to the spheno-occipital suture, a level which corresponds to a point near the anterior margin of the pituitary gland. In the twenty-nine rats which showed no increase in water-intake the scar on the skull was located below or above this level. Subsequent experiments have demonstrated beyond question that a puncture at this place produces the diabetic condition with a fair degree of certainty, but an absolutely accurate location of the significant point in the skull must wait until the vulnerable structure in the brain-stem has been definitely established by histological methods. And for the same reason, of course, the necessary depth of penetration cannot yet be discussed.

These experiments do not exclude the possibility that the results of the puncture may be caused indirectly through rupture of blood-vessels, or other interference with the circulation of the vulnerable area, rather than through the interruption of nervous pathways or the destruction of special nuclei.

As has been stated above, the increase in the water-intake produced by these brain-stem punctures is always permanent. It may or may not be very great, however, and there is considerable variation in the interval between the onset of the post-operative effect and the time when the maximum is reached. Because of these individual differences three curves will be presented.

The record in fig. 4 was obtained from the animal which showed the largest increase in water-intake. The water-intake in cubic centimetres is indicated on the ordinates and the age of the animal in days on the abscissæ. Before the brain-stem was punctured the average daily water-intake was approximately to 20 c.cm., and within the first two days after the operation it increased to 120 c.cm. On the fourth day it returned to the normal level, where it remained for that day only. A precipitous increase began on the fifth day, so that after two more days a level of over 200 c.cm. per day was reached. With the exception of a short interval of diminished intake occurring thirty-five days after the operation, this high level was maintained until the animal was killed six months later.

In another rat the increase in water-intake was not as great as in the previous record, but after the maximum level was reached it was maintained constantly to the end of the experiment. In this animal the puncture was not made with the scalpel, but with a thin probe to which a small steel loop was attached. A longitudinal opening was made in the skull with a scalpel before this instrument with the loop was inserted. It was whirled around once or twice before it was removed. The idea was to make a small circumscribed spherical lesion.

In the next record, fig. 5, the amount of 104 c.cm. was reached on the day following the operation. Thereafter for ninety days a gradual decrease occurred until a permanent level of 55 c.cm. was reached.

The water-intake of another animal increased steadily for seventy days after the puncture to 75 c.cm. daily and remained at this level fairly constantly until the animal was killed sixty days later.

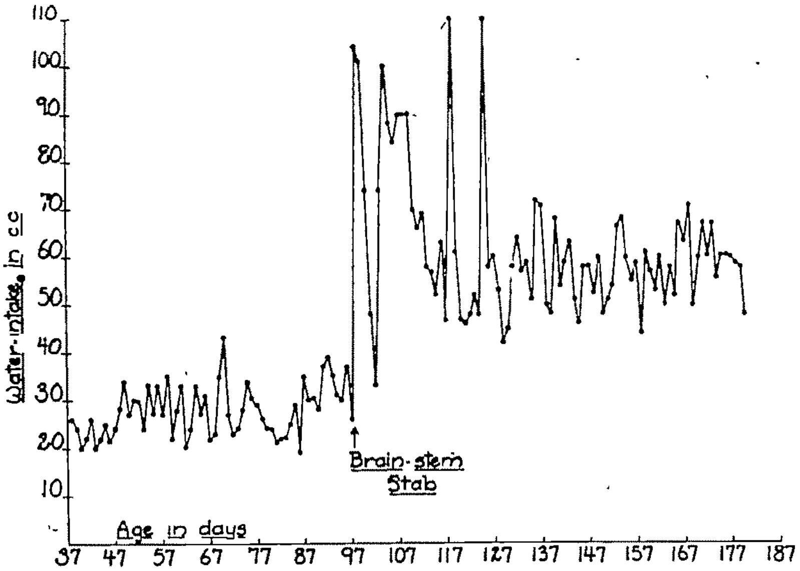

FIG. 5.—Record showing effect of brain-stem puncture. Rat 471.

In the animal the record of which is shown in fig. 6 no definite effect was noticeable for fifty days, except for a slight rise on the day following the operation. Then the water-intake increased steadily from day to day for sixty days, until a permanent daily level near 48 c.cm. was reached.

These graded differences in the effect of the puncture will undoubtedly be of value in the localization of the part of the brain responsible for the increase in water-intake. It is to be expected that in the rat of fig. 3 the puncture must have been made exactly in this area, for it is difficult to conceive of the production of a greater increase. In the other rats the puncture must have struck the area but not so fully as in the afore-mentioned rat.

The urine output of these animals was similarly increased. In the animal which showed the largest increase in water-intake (see fig. 3) the urine-output averaged about 10 c.cm. each day less than the water-intake, although the output was occasionally greater than the intake. The other animals showed approximately the same difference between water-intake and urine-output.

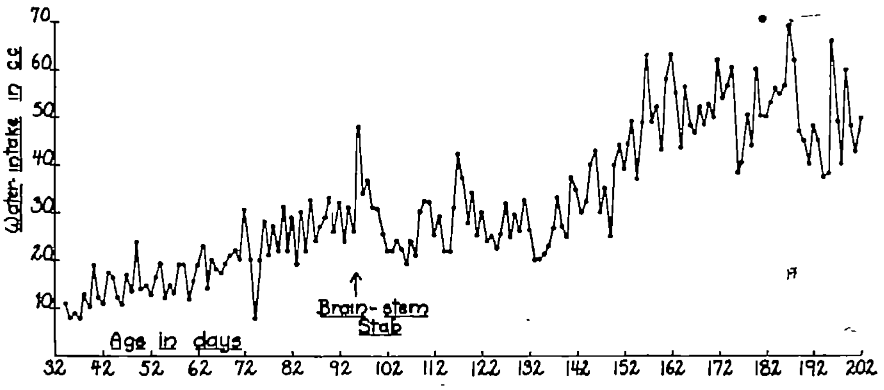

FIG. 6.—Further records showing effects of brain-stem punctures on water-intake. Rat 436.

While taking the records on urine-output, we were able to obtain information which may throw some light on the sequence in which the polydipsia and polyuria produced by the brain-stem puncture appear. Diurnal rhythms are known definitely to occur each day in both water-intake and urine-output. With this fact as a basis we believed that hourly records of the water-intake and urine-output might reveal which precedes the other. In this way it was established that usually the peak

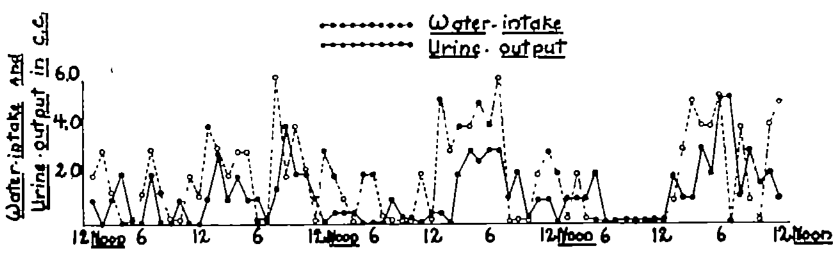

FIG. 7.—Chart of the hourly water-intake and urine-output for four successive days. Rat 430.

of the water-intake precedes the peak of the urine-output by one or two hours. A record of this kind from one of the diabetic rats is presented in fig. 7. It shows the water-intake and urine-output for four successive days, with the daily rise in both functions occurring between 12 midnight and 8 a.m., and the peak in water-intake preceding that of urine-output.

The other functions of the body were not consistently altered by puncture of the brain-stem. It seemed likely that there might be an increase in food-intake in the rats since occasionally a ravenous hunger is present in human diabetics in addition to the great thirst. However, the food-intake showed no change at all in any of the animals.

The body-weight showed no constant change. In two of the animals it decreased slightly, in one there was a slight increase and in the others no change at all.

Similarly the spontaneous running activity, as measured in the revolving drum, was not affected in any constant way. Animals which ran well before the puncture continued to do so afterwards, and those which were poor runners before remained inactive. The four- or five-day cycles of activity, characteristic of the female and associated with ovulation, were present in all of the seven animals at some time following the operation, but in four only were they as regular as they are in a normal rat. In the other three the activity showed marked irregular fluctuations.

Inasmuch as running activity is known to be closely associated with the function of the reproductive tract, being related to ovulation every fourth or fifth day, it was to be expected that when the running cycle occurred normal cyclical changes in the vaginal smear would be present also; and this was found to be the case. In the afore-mentioned three animals which showed additional long cyclical fluctuations of activity, however, the vaginal smears were markedly abnormal. During the interval when the activity was very low, the vaginal smears showed only the leucocytes and epithelial cells which are characteristic of the dioestrous condition of the reproductive tract. This picture of activity and vaginal smear is very similar to that found by Wang and Guttmacher (1927) in animals with injured ovaries. On the basis of this observation the conclusion may be drawn that in these three animals the pituitary gland was injured so that the function of the ovaries was disturbed and the running activity affected. In the other four animals it is very probable that there was no interference whatever with the normal functions of the pituitary gland.

It is of interest to note that in the animal with the largest increase in water-intake there was a marked loss of hair on the fore and hind legs and over part of the back, so that at the time this animal was killed the skin was entirely bare over these areas.

SUMMARY.

(1) It was shown that in the rat a marked and permanent increase in water-intake and urine-output may be produced by a fine puncture made in the brain-stem near the pituitary gland.

(2) The exact place was located in the skull through which a puncture with a scalpel regularly produces a polydipsia and polyuria.

(3) Although the effect is permanent, the curve of the increase varies considerably. The maximum increase may be reached on the first day after the puncture, or the increase may be very gradual, so that the maximum is not reached for several months afterwards.

(4) The increase in water-intake may be very great. One animal drank almost twice its body-weight each day.

(5) The effects produced by these brain-stem punctures are limited to the increase in water-intake and urine-output. There is no increase in food-intake, and body-weight remains unaffected. There are no constant changes in the spontaneous running activity or in the sexual cycles. One animal showed marked loss of hair on the inside of its legs.

(6) The absence of changes in the sex cycle suggests that the pituitary gland was not injured in these operations.

(7) Evidence is presented which indicates that polydipsia precedes polyuria.

(8) The nature and the localization of the lesion in the brain-stem will be described in a later paper.

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TUMOUR OF THE GASSERIAN GANGLION: SHEATH NEUROMA.[1]

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TUMOURS of the Gasserian ganglion of any type are uncommon, and most neoplasms that involve it arise from neighbouring structures and invade the ganglion secondarily. Only a small number of primary tumours have been placed on record, and on this account the following case seems worthy of description.

REPORT OF CASE.

Clinical features.—A woman, aged 28, came to the Mayo Clinic, May 20, 1929, complaining of anæsthesia and paralysis affecting the left side of the face. In 1924, for a period of three months, she had had sharp "jabbing" pains in the region of the left ear. A year later these pains had returned to the left ear and its vicinity for a period of six weeks, after which the pain had been replaced by a dull ache around the left eye, which had continued, with varying intensity, for two years. Two years before admission she had noticed that when she rubbed her lower lip a quiver, like an electric current, would begin in the left ear; this had been accompanied by pain in the same region, at times very severe for a few seconds. Two and a half years previously the muscles of the forehead had become paralysed, and at the same time she had had some discomfort, associated with crackling noises, in the left temporomandibular joint. Gradually anæsthesia had developed, until about one and a half years before admission there had been left-sided anæsthesia which had affected the forehead and anterior part of the scalp, the eye, the cheek, the nose, both upper and lower lips, the lower jaw, the tongue and the roof of the mouth. Preceding each advance of the anæsthesia there had been severe transitory pain in the area to be affected. During the same period paralysis of the left side of the face developed. For the last year, also, the patient had had a sensation as of stopping up of the Eustachian tube, and for the last six months an impression of obstruction in the left side of the nose. In the last ten months she had had thirty corneal ulcers in the left eye. Eighteen

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months before admission she had been very drowsy for a few months; she said she could sleep anywhere, at any time.

Examination disclosed complete paralysis of the peripheral type of the left fifth and seventh nerves, except that a little power remained in the platysma, no doubt due to the presence of anastomoses between the second and third cervical nerves and the inframandibular branch of the facial nerve. Auditory acuity was normal on both sides. There was loss of taste on the anterior part of the left side of the tongue. The corneal reflex was absent on the left side. The movements of the left half of the soft palate were perhaps a trifle less free than of those of the right half, but there was no difference between the palatal reflexes, and no paralysis of the pharyngeal muscles. The fundi and visual fields were normal.

The association of pain and, later, anæsthesia in the territory of the fifth nerve suggested that a destructive process, probably neoplastic, was active in the cave of Meckel; and the paralysis of the seventh nerve, which included the fibres derived from the nervus intermedius, made it likely that the process had transgressed the middle fossa of the skull and was active in the posterior fossa. On the other hand, if the tumour were pressing on the seventh nerve and the nervus intermedius in the posterior fossa, it was extremely difficult to explain the escape of the fibres of the left eighth nerve, which were repeatedly shown to be intact. We considered the possibility of extracranial extension of the tumour through the foramen ovale, but we were unable to demonstrate this clinically; nor was there any radiographic evidence of destruction of bone in this region. A third route by which such a process might have reached the facial nerve was by erosion of the petrous part of the temporal bone until it involved the Fallopian canal; but of this there was no radiographic evidence. We concluded that the tumour, growing down from the cave of Meckel toward the upper part of the internal meatus of the ear, involved first the facial nerve and then the nervus intermedius, and that possibly, as is the case with conducting fibres generally, the efferent motor nerve was more sensitive to the pressure of the neoplasm than was the afferent sensory nerve. The feeling of stuffiness in the Eustachian tube could be explained by its infiltration by tumour cells, since the cartilaginous part of the tube is in close proximity to the foramen ovale. On the other hand, it might have been due to paralysis of the tensor tympani muscle, as a result of the destruction of the nerve fibres passing through the motor root of the fifth nerve to the otic ganglion.

Surgical features.—The surgical problem which presented itself was to decide which cranial fossa should be investigated first. As the pain had preceded the facial palsy, we decided to begin by exploring the middle fossa, as for section of the sensory root of the fifth nerve; if necessary, we intended to explore the posterior fossa at a subsequent date. The patient had returned home for a period, and exploration of the middle fossa was carried out, June 24, 1929. When the ganglion was exposed, its third and second divisions and the ganglion itself were seen to be of a dark maroon colour, and the dura over the ganglion was much more adherent than normally. When the arachnoid over the sensory root was opened, the fibres of the root were at first indistinguishable, as they were surrounded by maroon-coloured gelatinous material. Portions of this material, and a certain amount of tissue from the posterior margin of the ganglion, were removed for histological examination. This procedure revealed that the ganglion had been pushed forward, so that instead of passing downward and forward to reach the foramen ovale, the third division of the fifth nerve passed downward and backward. There was no evidence of infiltration of the petrous portion of the temporal bone to explain the paralysis of the seventh nerve. As complete removal of the tumour was obviously out of the question, the operation was completed by passing a gauze drain down to the ganglion and closing the wound in layers. The latter procedure was somewhat difficult, as the temporal muscle was so atrophied and friable that its approximation was unusually tedious. The patient had a speedy convalescence; she sat up on the third day, and left the hospital on the fourth day for a neighbouring convent. It was decided not to perform the suboccipital decompression unless symptoms of increased intracranial pressure should appear at a later date.

When the patient was last heard from, October 11, 1929, she had resumed teaching, was in good health, and had not suffered any disability from the exploration.

Pathology.—The cells of the tumour were small, with a slight amount of agranular cytoplasm; the nuclei almost filled the cells. The majority of the nuclei were oval or irregular, and stained deeply with hæmatoxylin or thionin; a few still more deeply staining granules also were present. The nuclei did not contain nucleoli. The cells did not show processes when stained with Mallory's phosphotungstic acid hæmatoxylin. The cells of the tumour were arranged in columns and in tubules (Plate X, fig. 1). The peculiarly-formed tubules or alveoli were mainly composed of two concentric rings of cells, with the longer axes of the nuclei pointing toward the centre of the alveolus (fig. 2). This arrangement was present throughout, except in the solid columns of cells, in which the nuclei in the centre had no definite arrangement, although the peripheral nuclei were frequently arranged in palisade-like rows with their longer axes parallel to each other (fig. 3). Few mitotic figures were present, and few normal ganglion cells were found, but there were some degenerated cells and remnants of cells in which a little chromatin substance could be demonstrated with the toluidin blue stain. In some of the alveoli formed by the peculiarly arranged tumour cells, remnants of ganglion cells were seen, but normal cells were not so surrounded. Occasionally beginning proliferation of the endocapsular cells was noted, and in such regions there was beginning degeneration of the ganglion cells (fig. 4). The supporting structure was increased in amount, but not to an excessive degree, and in parts it had undergone hyalinization. Psammoma bodies were rare; only one was seen in all the sections studied, and contrary to the findings of most other observers of tumours of the Gasserian ganglion, plasma or other inflammatory cells were not found. There were many bundles of nerve-fibres here and there, broken up by columns of tumour cells, and the axis cylinders of such bundles showed degeneration.

The cells composing the tumour simulated somewhat those normally seen in the arachnoid, and called arachnoid cell clusters. However, the latter are differently arranged and have more cytoplasmic processes; they form whorls, with a heavy supporting structure, and psammoma bodies are abundant. On the other hand, in this tumour neither whorls nor psammoma bodies were to be seen. The cells of the tumour strongly resembled those which occur in the capsule of the normal cell of the Gasserian ganglion The possibility that such cells can produce a tumour was first recognized by Marchand.

In Marchand's case the cells of the tumour and their arrangement and relation to the ganglion cells were similar to those in the case described here. Marchand stated: " These cells are identical with the capsule cells of the ganglion cells." Similar cases have been described by others, under various names, such as alveolar sarcoma (Krepuska), or endothelioma (Sachs and Rand), but their possible origin from ganglionic capsular cells has not been discussed. Marchand reviewed the literature of tumours of the Gasserian ganglion, and found a few cases like his own which had been otherwise classified. Sachs reported a tumour which, from his description, was of the same nature as that reported in this paper; the tumour cells were arranged around " empty spaces in which ganglion cells had been lying, but no traces of the cell remained." He classified it as an endothelioma.

In a case described by Dercum, Keen and Spiller, Spiller observed that when the tumour (an endothelioma) invaded the Gasserian ganglion many nerve-cells were destroyed and there was proliferation of the capsular cells. Spiller considered this picture to be secondary to that of invasion of tumour and destruction of ganglion cells. Krepuska, earlier than Marchand, described a tumour which histologically was an alveolar sarcoma and was similar to that in the case described in this paper. More recently Rand reported a case which he stated was similar to that of Marchand, and in which he classified the growth as an endothelioma.

The origin of the ganglion capsular cells is uncertain, and on this account it is easy to understand the confusing terminology used in classifying tumours arising from them. Lenhossek said that these capsular cells " consist of connective tissue which passes into the sheath of Henle of the axis cylinder process."

Marchand considered the cells similar to the cells of the sheath of

Schwann, or indifferent endothelial cells. As pertaining to this the experiments of Harrison may be noted, in which he removed the ganglionic crest of *Amblystoma punctatum.* Motor nerves developed with axis cylinders, but without cells like those in the sheath of Schwann. Harrison said, "Sheath cells are not mesodermal, but arise for the most part from the ganglionic crest in connection with the spinal ganglia," and, "the sheath cells are to be regarded as the neuroglia of the peripheral nerves." However, Bartelmez and Evans stated: "In no form have they (neural crest cells) been followed with certainty from their origin to their differentiation into ganglion, sheath and capsular cells." Stout described a tumour of the ulnar nerve which, like most sheath neuromas of the Gasserian ganglion, had produced metastasis in the regional lymph nodes and had also formed some rosettes. Some "schwannomas" of the peripheral nerves are similar to the tumour described here.

Until a definite origin is assigned to the ganglionic capsular cells, it seems best to classify this tumour as a sheath neuroma, and although it has some similarity to the neurocytoma of the retina, it will possibly be ultimately classified with the gliomas.

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PLATE X.

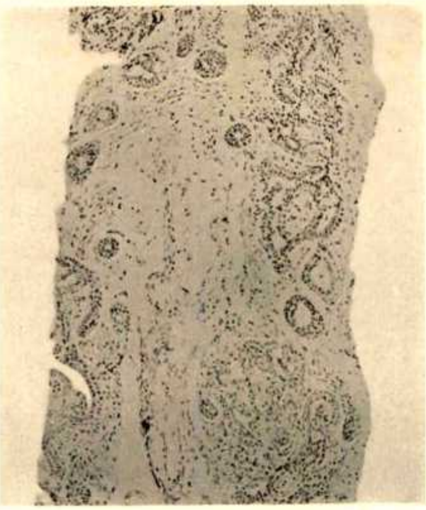

Fig. 1.

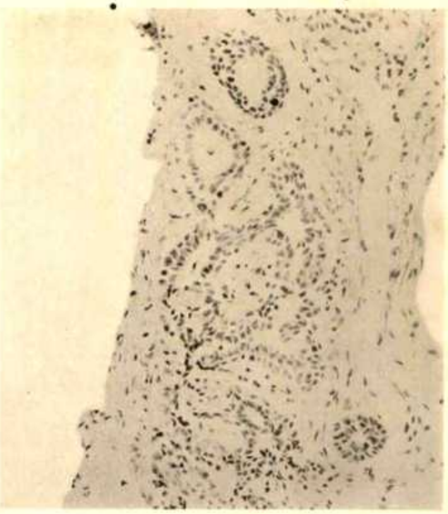

Fig. 2.

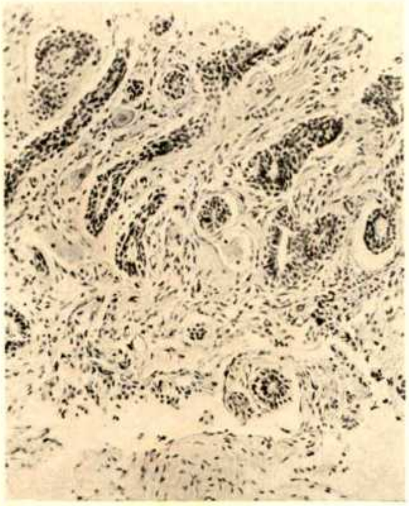

Fig. 3.

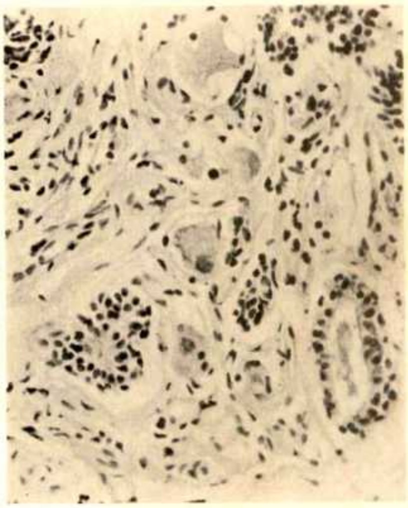

Fig. 4.

To illustrate paper by James R. Learmonth and James W. Kernohan.

[10] STONE, L. S. "Experiments on the Transplantation of the Placodes of the Cranial Ganglia in the Amphibian Embryo. IV. Heterotopic Transplantations of the Post-auditory Placodal Material upon the Head and Body of *Amblyostoma punctatum*," *Journ. Comp. Neurol.*, 1929, **48**, 311-330.

[11] STOUT, A. P. "A Tumour of the Ulnar Nerve," *Proc. New York Path. Soc.*, 1917-19, **17-19**, 1-12.

DESCRIPTION OF ILLUSTRATIONS, PLATE X.

FIG. 1.—Section of tumour showing the arrangement of the tumour cells in tubules and columns. The comparatively acellular supporting structure is seen. (Thionin stain, × 150.)

FIG. 2.—A portion of fig. 1 showing the two rows of tumour cells forming the tubules or the columns; no mitotic figures are seen in this field. (Thionin stain, × 300.)

FIG. 3.—This area shows tumour masses similar to those in figs. 1 and 2, but with ganglion cells in the supporting structure; the lumina of the tubules are empty except for débris. (Hæmatoxylin and eosin stain, × 175.)

FIG. 4.—The ganglion and capsular cells are intermingled with the tumour cells; two ganglion cells show proliferation of the capsular cells; these cells show early signs of degeneration. (Hæmatoxylin and eosin, × 350.)

NOTICES OF RECENT PUBLICATIONS.

Lewandowsky's Handbuch der Neurologie. Ergänzungsband; 1ster Teil, 4ter Abschnitt. Die traumatischen Läsionen des Rückenmarkes auf Grund der Kriegserfahrungen. Von O. FOERSTER. 1929. S. 207. Berlin: Julius Springer. Price 39 Marks.

Previous volumes in this series have already been reviewed in this Journal and in the present Professor Foerster continues his detailed collection and analysis of war injuries of the nervous system.

The high opinion of this comprehensive work expressed in respect of previous volumes is equally deserved by the present section. In this the author gives a detailed account and analysis of a large series of personally observed cases of war injury of the spinal cord, and has collected all similar cases reported in neurological literature since 1914. The enormous mass of information thus assembled does not make easy reading, and the great value of the book will be as a comprehensive and accurate work of reference.

The author does not deal primarily with the symptomatology of war injuries of the cord, but is concerned with the various ways in which gunshot wounds, stab wounds, explosions, electric shocks and the numerous forms of bodily injury may produce lesions of the spinal cord. Thus direct injury to the cord, injuries of the vertebral column, of the limb girdles, falls and blows on the back are all considered in relation to the types of spinal cord lesion that may be associated with them. In the second section of the book, the minute anatomy of these cord lesions, recent and late, and the secondary processes resulting from them are described in detail.

The author has produced a complete record of the various kinds of bodily injury which may result in spinal cord lesions, and of the pathological anatomy of such lesions.

Les Acrocyanoses. Par F. LAYANI. Paris: Masson et Cie. 1929. Pp. 280. Price 32 francs.

The syndrome with which the author is concerned affects the extremities and consists in cyanosis, coldness, sweating and subcutaneous thickening. It is a painless and unvarying condition, not leading to gangrene, blistering or "deadness" of the extremities, and is thus seen to differ from Raynaud's disease and thrombo-angeitis obliterans. Allied, but differing conditions are Raynaud's disease, erythromelalgia, sclerodermia, recurring phlyctenulosis, various œdemas and urticaria. Associated symptoms are sometimes found, such as sensory impairment of the affected regions and local muscular atrophy.

The condition is commonly found in association with hereditary vasomotor instability, and sometimes in tuberculous subjects and in the subjects of hereditary syphilis.

The author regards disorders of endocrine function as primarily responsible, but there appears to be no information as to which gland is most concerned or the nature of its dysfunction. There is, in other words, the usual vagueness which characterizes hypotheses invoking endocrine disorders. The immediate cause of the condition is capillary stasis from defective sympathetic nervous activity. With etiological and pathological knowledge so vague and speculative, it follows that indications for treatment are also of a somewhat unconvincing character.

Études sur les Maladies familiales nerveuses et dystrophiques. By O. Crouzon. Paris: Masson et Cie. 1929. Pp. 382. Price 55 francs.

This volume is an elaboration of Dr. Crouzon's valuable article on the subject contributed to the "Traité de Pathologie médicale et de Thérapeutique appliquée." Part I is concerned with the familial affections of a strictly neurological order, and the clinical features of a very large number of syndromes—rare and common—are ably set out. Two or three conditions are included as "nervous disorders, exceptionally familial," amongst which one is surprised to see von Recklinghausen's disease. The second part deals with dystrophic familial affections, which include cranio-facial dysostosis, cleido-cranial dysostosis, familial pleonosteosis, and heredity osteopathy. Dr. Crouzon's book is valuable for the purpose of reference, and he has dealt with a great number of obscure and transitional cases which have appeared sporadically in the literature.

The encyclopædic value of this monograph is very seriously vitiated, however, by the lack of a proper bibliography, a feature which is essential in a work of this character.

The Mechanism of the Larynx. By V. E. Negus. Pp. 528. London Wm. Heinemann, Ltd. 1929. Price 45s.

In this exhaustive monograph, the author has dealt with the embryology, the comparative morphology and the physiology of the larynx. The subject matter is almost entirely original, although the work of other investigators in this field is fully discussed and incorporated. He emphasizes that speech is not the only activity of the larynx, nor even one of its more important functions. He traces the structural alterations in the complexity of the larynx which have evolved to meet the habits and needs of the species, and the modifications in its anatomy brought about by the functions of olfaction, respiration and deglutition, and the development of prehensile forelimbs. Finally, the author leads up to the problem of the employment of sound as a means of communication amongst the animal creation, and thence to the function of the larynx as an instrument of phonation.

The Autonomic Nervous System. By ALBERT KUNTZ Pp. 569. London: Baillière, Tindall and Cox. Price 31s. 6d.

There is a rapidly growing interest in the problems attendant upon the study of the sympathetic and parasympathetic nervous systems, as illustrated by the quantity of research at present carried out on their anatomy and physiology.

Unfortunately there are few comprehensive monographs which are in accord with modern conceptions. Dr. Kuntz's book, therefore, fills a very real want. The plan of this monograph comprises first an anatomical and histological discussion of the autonomic nervous system; the general physiology is next dealt with, and he afterwards deals with special physiological details as the innervation of the heart, blood-vessels, the respiratory, alimentary and biliary systems, the internal and external secretory glands, the uro-genital apparatus, the eye and the striped muscles. Two chapters are devoted to general and special pathology. There is a useful discussion on the mechanism of visceral pain, and the conception of Eppinger and Hess of vagotonia and sympatheticotonia is critically discussed, and is regarded as a useful working hypothesis. A section on the surgery of the autonomic system concludes the volume. There is an excellent bibliography to each chapter, and each section is concluded with a judicial exposition of the various problems which have been dealt with in the text. A chapter on the methods of investigation of the sympathetic nervous system, as practicable to the clinician, would have been useful.

La Maladie de Friedreich. By P. MOLLARET. Pp. 308. Paris: Amédée Legrand. 1929.

This volume represents the most complete monograph available on the clinical aspects of Friedreich's ataxia. The author does not deal at all with the pathology of the disease. Each of the classical signs and symptoms is treated exhaustively with frequent reference to the author's personal series of 21 cases. Among the rarer clinical features which are studied may be mentioned affections of the auditory nerve, strabismus, optic atrophy, visual complications, psychical changes, hepatic efficiency, and abnormalities in the spinal fluid. A useful section is given on the course of the disease, the frequency of remissions and the mode of dying of these patients. Atypical cases are considered under the following four groups: (1) Forms with muscle atrophy; (2) the *formes frustes*; (3) transition types linking classical cases of Friedreich's ataxia with Marie's ataxia on the one hand, and familial spastic paraplegia on the other; and (4) cases in association with other neurological syndromes, in particular myopathy, idiocy, Huntington's chorea and hysteria.

An excellent bibliography concludes this monograph. Dr. Mollaret's book is valuable as a work for reference, but a detailed and voluminous monograph on what is after all an artificial pigeon-hole for the great group of familial ataxias is out of accord with the modern conceptions of neurology. What is required is a broadminded effort to collect and study the classical subtypes of this group as a whole rather than a segregation and study of individual cases in rigid walled compartments.

Études cliniques sur les Syndromes moteurs et Réflexes de la Paroi abdominale et d'Origine cérébrale. Par AKE BARKMAN. S. 302. Upsala: Almquist and Wiksells.

In a long historical introduction the author attempts to show that in the evolution of our conceptions of localization in the fore-brain it has been the clinician rather than the experimental physiologist or anatomist who has first perceived the truth; and that the current conceptions concerning the cerebral representation of the muscular activity of the abdominal wall are completely at variance with the conclusions which he sets forth in this volume.

In Part II he reviews briefly the anatomy and individual action of the abdominal muscles, and then presents in some detail his methods of investigation and the results of his examination of 135 normal adults. In Part III are given the analyses of the findings in 65 cases of cortical, subcortical, or capsular lesions of the pyramidal tracts. The author concludes that in cerebral hemiplegia the abdominal muscles are involved constantly and permanently. This hemiparesis is best observed by the deviation of the umbilicus and arching of the mid-line to the normal side during performance of the test movements, especially by forcible retraction of the abdomen. It was frequently observed even when the abdominal reflexes were symmetrical, or obtainable on neither side. It was demonstrable by these methods in a few patients in whom all other signs of a pre-existing hemiplegia had completely cleared up.

The author concludes that there is cortical representation of the movements of the abdominal wall, and that this representation is further subdivided into at least two centres, one for the upper and one for the lower quadrant. He believes that the essential region must lie precisely between the centres for the hip and shoulder.

L'Hyperostose frontale interne: Syndrome de l'Hyperostose frontale interne avec Adipose et Troubles cérébraux. Par F. MOREL. Pp. 95 avec 13 figures Paris: G. Doin. 1929. Price 20 francs.

The extreme but irregular thickening of the inner surface of the frontal bone which is occasionally visible in radiographs of the skull is fully and carefully described in this small monograph. It is generally found in advanced age, and seems to be commoner in women than in men. It is usually a chance radiographic or pathological finding, but it is not infrequently associated with clinical symptoms, as adiposity, disturbances of sleep, polyphagia, polydipsia, general asthenia, severe headaches and sometimes senile epilepsy. There is evidence that it is related to disturbances in the infundibulo-tuberian region, and that the essential factor in its pathogenesis is a disturbance in the calcium metabolism. Its localization is explained by the tension of the dura mater on the frontal bone.

This volume is well illustrated by radiographs, and the literature on the subject from the days of Morgagni is fully reviewed.

Handbuch der Geisteskrankheiten. Herausgegeben von OSWALD BUMKE. Siebenter Band. Spezieller Teil III. S. 700 mit 74 Abbildungen. Berlin: Springer. 1928. Price 66 Marks.

The study of the exogenous reaction-types and the organic psychoses has been so much influenced by the work of Bonhoeffer that the present volume, which deals with these conditions, may be regarded as a monument to him. In an excellent introductory essay Stertz points out how Bonhoeffer's examination of the symptomatic psychoses led to his description of the now familiar "exogenous types of predilection," and later to his disputable hypothesis of intermediary factors (ætiologische Zwischenglieder), secondary to metabolic changes. The extension of Bonhoeffer's findings to the organic psychoses, which are really "exogenous disorders that have become chronic," is discussed at some length: in these, it is concluded, dementia is the "axial syndrome" and the familiar exogenous types are "peripheral." Stertz puts forward his view that Bonhoeffer's various exogenous types of reaction are not of equal diagnostic value and can be classified as including obligatory or fundamental symptoms, and facultative or accessory symptoms, dependent for their appearance on various conditions and likely to occur also in endogenous disorders. The influence of factors such as premorbid personality, age and constitution generally, is discussed, as well as the extent to which mental disorders of endocrine origin conform to the exogenous type of reaction. In the endogenous dementing processes, epileptic and schizophrenic, the same principles as in the "organic" disorders are held to apply.

Ewald gives an exhaustive clinical account of the exogenous forms of reaction, classified as delirious disorders, twilight states, "amentia," hallucinatory forms, and then the post-psychotic conditions. He next describes in detail the mental changes seen in individual disorders of the thoracic and abdominal organs, the blood, the ductless glands, &c., as well as in the infectious diseases, with a brief appendix on the generative psychoses of women, in which the psychological factors are too little considered. Ewald agrees with Bonhoeffer that there is little hope of being able to recognize the ætiology of symptomatic psychoses solely from a study, however careful, of their form; for this the somatic accompaniments will be much more valuable.

Psychoses due chiefly to exogenous toxic substances are dealt with by Meggendorfer. These psychoses, he holds, must be regarded as the product of a biological interaction between the poison and the poisoned organism. The implications of this are gone into thoroughly; then the various poisons are taken in order, alcohol and morphia being dealt with very faithfully, as might be expected in view of their importance. Industrial poisons also receive adequate consideration.

Mental changes following injury to the brain are described by B. Pfeifer, who also writes on psychoses associated with meningitis and cerebral tumour. The common belief that "Witzelsucht" is characteristic of tumours of the frontal lobe is incidentally laid by the heels.

The section by W. Runge on psychoses in other disorders of the brain than those just referred to, contains a thorough exposition of the psychic changes in encephalitis lethargica. Disseminated sclerosis, Schilder's encephalitis, extrapyramidal disorders, abscess, hæmorrhage and softening are considered also. These sections consist largely of useful summarizations of the literature, reliable but tedious.

Throughout the book prognosis and treatment are not neglected; the sections on drug addiction are particularly informative in this connection.

Das Schizophrene Denken. Von JAKOB FROSTIG. S. 187. Leipzig: G. Thieme. 1929. Price M. 4.

The subtitle of this book indicates that it is an attempt to study the "nonsensical" utterances of the schizophrenic from a phenomenological standpoint. The phenomenology which the author means, however, is that of Husserl, rather than of Jaspers; the work is consequently philosophical, not clinical, and seems hardly likely to be of interest to English psychiatrists.

The discussion, though severely abstract and theoretical, is not obscure. It is, however, such as scarcely to lend itself to brief exposition. The author's main conclusion is that whereas for normal people words serve to "signalize collective structures" (the essential features through which we experience objects as being), for the schizophrenic this is no longer the case; there is in him a general inability to actualize collective structures and the elements of consciousness which appertain to these structures.

Die psychischen Reaktionsformen. Von HARRY MARCUSE. S. 262. Berlin: S. Karger. 1929. Price M. 22.

This work is an expansion of the author's previous contributions to an "energetic theory of the psychoses." His theoretical views, which bulk largely, are based on the psychological teachings of Jodl.

Mental happenings are for him reactions to stimuli, divisible into primary and secondary, according as the stimuli are "presentative" and actual, or past and now reproduced, leading to ideas. In addition to the stimulus, the "psychic constitution" is recognized as important, i.e., the manner of reacting to stimuli, and the distinguishing feature here is said to be the "intensity" of the psychic activity. Constitutions are classified accordingly. The author holds that there is one somatogenic psychosis which includes schizophrenia, paranoia and manic-depressive insanity, the ætiological agent being a hypothetical "catatonic noxa," the reaction to which depends on the mental constitution of the affected person. Hypnosis is given as a valued means of differentiating psychogenic from somatogenic reactions and of treating the former. Chapters on simulation, dreams and general cultural questions complete this ingenious but unconvincing attempt to rearrange the psychoses on the basis of a psychological theory.

Die Psychologie der Schizophrenen. Von CARL SCHNEIDER. S. 301. Leipzig: Georg Thieme. 1930. Price M. 25.

The author's views on schizophrenia are here set forth more fully and consecutively than in his earlier papers, which have met with a good deal of criticism. The present work has profited from this, and provides a useful exposition of the problems of schizophrenia as well as a stimulating attempt at their solution. There is no concealment of the difficulties and gaps in this; it is not even maintained that psychopathological investigation establishes schizophrenia as a "disease-unity," but the author has more or less accepted the current clinical conception of the disorder and confined himself to clarifying its psychopathology.

In the beginning he considers the frequency with which the most important schizophrenic symptoms were met with in 408 carefully observed cases of his own. He then gives an excellent critical review of the present views on schizophrenia, and considers the relationship between the symptoms of this disorder and the experience of falling asleep. The similarity, which had previously been pointed out by Kraepelin and Bumke, is considerable and provides the starting point for the development of the author's views. He examines the various common symptoms, "primary" and "accessory," and concludes that other features than these are the true characteristics of the psychic life and expression of the schizophrenic. Bodily changes he disposes of as nosologically unimportant; search after causes is equally useless from this point of view. He is equally critical of the studies in physique and personality so far as they bear on this problem. He concludes with a brief but valuable section, on the course, prognosis, delimination, diagnosis in the individual case, and treatment of the disorder.

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of "Brain." If reprints are required in pamphlet form, with wrapper, title-page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BALE, SONS & DANIELSSON, Ltd., 83-91, Great Titchfield Street, London, W.

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EDITOR.

JULY, 1930.

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BRAIN.

PART 2, VOL. 53.

THE STRUCTURAL BASIS OF TRAUMATIC EPILEPSY AND RESULTS OF RADICAL OPERATION.[1]

BY O. FOERSTER,
Breslau,
AND
WILDER PENFIELD,
Montreal.

EPILEPSY is a specific reaction on the part of the central nervous system to a noxious stimulus. It may be called focal when it is possible to determine a circumscribed area upon which the stimulus first acts. Thanks to recent advances in neurophysiology and in neurosurgery it is now possible to include in the group of focal epilepsy many cases formerly considered to be generalized. In addition to the march of crude motor phenomena characteristic of Jacksonian epilepsy, alterations in the directions of gaze, turning of the head and certain sensory auras may serve to point to the focus from which an epileptogenic stimulus is derived.

Even in traumatic epilepsy, however, where the irritative focus may be easily localized there are other factors to be considered. In addition to the irritative stimulus the occurrence of a convulsion depends upon the irritability and the susceptibility of the brain to such stimulus. Further, there are certain general influences which though they operate from a distance directly influence the production of convulsions. There can be little doubt but that epilepsy is an active stimulation process and not a release phenomenon, although release phenomena may be observed during and following an attack.

Exploration of the human cerebral cortex, both in normal and pathological areas in well over 100 cases under local anæthesia, has made it possible to outline certain definite epileptogenic cortical areas (Foerster [4]). The areas in the human cortex are analogous to but not identical with the areas outlined by Vogt in monkeys. The movement patterns which follow such stimulation experiments provide a local sign which often makes it possible to localize the irritating focus of an epileptic discharge, even where there are no physical signs to suggest this localization.

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[1] Read before the Association for Research in Nervous and Mental Disease, New York, December 2, 1929.

This is a partial presentation of a monograph which will appear shortly *in extenso* in the *Zeitschrift fur die gesamte Neurologie und Psychiatrie.*

Quantitative stimulation in the post-central field (3, 1, 2) (fig. 1)

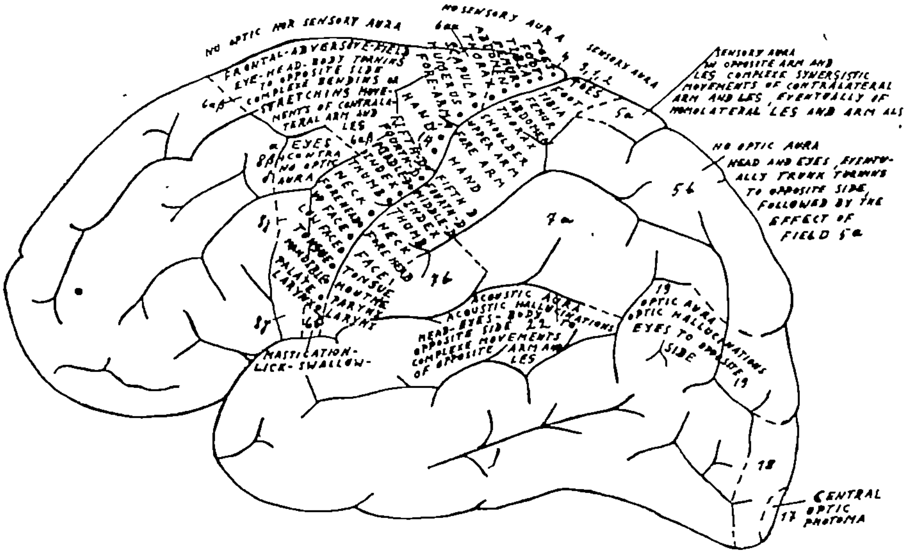


FIG. 1.—Epileptogenic cortical areas in the human brain. The outlines indicate roughly the initial movements and auræ which follow direct stimulation of the cortex by an electrical current sufficient to produce an epileptic seizure.

requires a considerably larger amount of current to bring on an attack than in the pre-central (4 + 6a α). The clonic convulsion produced by stimulation in either area appears to be about the same. If it arises, however, behind the central fissure the attack is preceded by a sensory aura which begins in the part first affected and often spreads like a wave over that side of the body.

Stimulation in the frontal adversive field (6a β) (fig. 1) produces turning of eyes, head and body to the opposite side, followed by clonic or tonic movements of the contralateral arm and leg. These movements take place without any aura. Below this field the frontal eye field may give rise to a convulsion initiated by isolated clonic turning of the eyes to the opposite side without any optic aura. Following this the attack takes on either the characteristics of a frontal adversive field attack, or a simple pre-central attack, depending upon the direction in which the stimulus spreads.

Stimulation of the occipital pole in area 17 produces an attack which is ushered in by an optic aura such as light, flames, stars, &c., usually in the opposite visual field. Stimulation farther forward (area 19) causes a change in the direction of the gaze to the opposite side associated with an optic hallucination, such as a figure in the opposite visual field. A stimulus in the parietal adversive field (5b + 5a) produces turning of the eyes, head and body to the opposite side and movements of the opposite limbs. If it be in the anterior portion of this area (5a) the movements of the head and eyes may be absent, but there is a sensory aura of discomfort in the arm and leg of the opposite side followed by leg and arm movements. As indicated in fig. 1, a stimulus in the posterior temporal region is likely to produce an acoustic aura. Lesions affecting the operculum centrale (area 6b) cause grunting, licking, swallowing or some such movement of the mouth and pharynx, associated usually with a sensation in this vicinity and also singultus.

In any case of focal epilepsy where there is a reasonable suspicion of a cerebral lesion, *encephalography* should be employed to demonstrate any gross cerebral abnormality. If operation be then undertaken a careful electrical exploration of the cortex under local anæsthesia serves to prove whether or not the suspected focus is actually the site of the initiation of the discharge.

The radical excision of a lesion, even though it is obviously the focus for epileptic discharges, can only be a rational procedure if the lesion produced by the excision be a more innocent one than the original focus. A comparison of the results of cerebral laceration and excision has been made the subject of a series of experiments by Penfield [1] which indicate a striking difference in the end-result of excision from that of laceration.

If a wound be made in the brain and the damaged cerebral tissue is not removed there forms rapidly a scar which contains connective tissue and fibrous astrocytes, and which is densely attached to the overlying meninges. A very rich plexus of new-formed vessels appears in the scar. This plexus anastomoses on the one hand with the extra-cerebral blood supply of meninges and scalp, and on the other hand with the vessels of the brain. The cicatrix contracts steadily over a period of years. There results a very considerable pull upon the vaso-astral framework of the brain. This framework is made up of the blood-vessels and attached fibrous astrocytes. The pull exerts an influence on the whole hemisphere and, in fact, upon the whole brain.

The effect of such a pull after a brain injury has been pointed out by Foerster [2]. He noted that there was a "wandering" of both lateral and third ventricles towards the site of such a lesion. The cause of this phenomenon is now apparent, as will be pointed out below. The displacement is due to cicatricial *pull* probably associated with the atrophy which takes place in the brain about the cicatrix.

Excision of cerebral tissue, however, produces a different result. There is no organization of connective tissue. Instead of that there appears a fluid-filled space with a very small amount of gliosis about it, without a plexus of new-formed vessels and without evidence of cicatricial pull upon the surrounding brain. Thus the results of brain injury and brain excision are structurally quite different.

Nevertheless, in the last analysis of course, the wisdom of substituting a non-contracting fluid-filled space for a contracting cicatrix in these patients must be judged on a human empirical basis.

The cases to be reported below provide an opportunity for studying the result of the excision of cerebral cicatrix in epileptics and the mechanism involved. In the group of cases selected the gunshot wounds of the brain are of long duration and the birth injuries of still longer. Consequently the excised tissue offers a remarkable opportunity to study the late results of cerebral trauma histologically.

CASE REPORTS.

Case 1.—In 1914 the patient received a gunshot wound in the left parietal region. This was followed by twelve hours of unconsciousness and a hemiparesis and hemi-ataxia of the extremities of the right side. Ataxia and intention tremor have persisted in the right arm together with loss of cortical sensibility. The patient learned to write with his left hand. The onset of Jacksonian epilepsy involving the right side began in 1920, i.e., six years after the trauma.

Encephalography in 1925 showed some enlargement of the left lateral ventricle and a displacement of both lateral and third ventricles towards the side of the lesion (fig. 2).

Operation, 1925.—A large parietal craniotomy was carried out and dura mater was found to be densely adherent to an underlying brain scar. Within the scar was a large cyst which did not communicate with the ventricles. Electrical exploration showed the lesion to lie just posterior to the motor area for the fingers. A wide excision was carried out as indicated by the broken line in fig. 3. The bone flap was not replaced. The patient made a good recovery and in the five years following the operation up to the time when last heard of he was quite free from convulsive seizures.

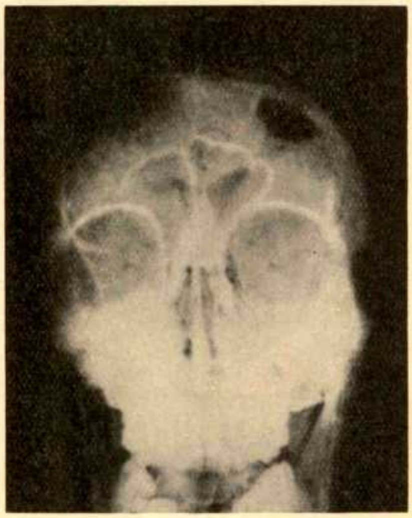
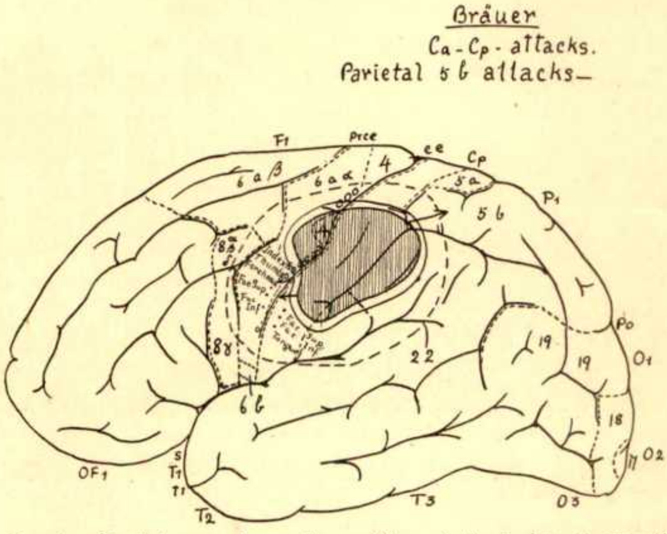


FIG. 2.—*Case* 1. Encephalogram (brow up) eleven years after gunshot wound of left parietal region. Cranial defect is shown and lateral ventricles pulled towards it.



Bräuer
Ca - Cp - attacks.
Parietal 5 b attacks—

FIG. 3.—*Case* 1. Shaded area shows the position of the lesion at operation and the second line the extent of operative removal. The pattern of the attacks indicated that the stimulus might arise in front of or behind the lesion, as indicated by the arrows.

The gross specimen showed considerable thickening of the dura. A bit of bone was embedded in the cicatrix and bands of fibrous tissue could be seen passing downwards into the brain (fig. 4).

Microscopical examination shows the connective tissue to be entering the brain scar in more or less parallel lines (fig. 5). Closer examination shows these bands to be made up of blood-vessels and sturdy collagen fibres. When stained so as to demonstrate both collagen fibres and neuroglia fibres, it is seen that the two types of fibres are more or less intermingled and parallel as though they were strands in a rope. Deeper in the brain neuroglia fibres are found lying in parallel lines, pointing upwards towards the meningo-cerebral adhesion (fig. 6).

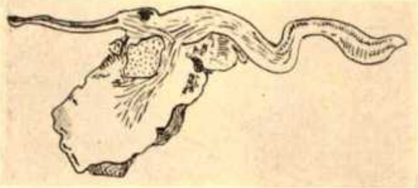


FIG. 4.—*Case* 1. Cross section of cicatrix attached to thickened dura.

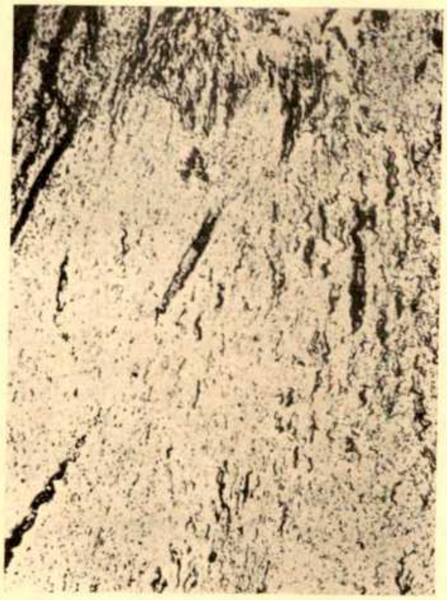


FIG. 5.—*Case* 1. Connective tissue and vessels entering the brain scar in parallel strands. Silver carbonate collagen stain.

In one sense this tissue can no longer be called cerebral tissue inasmuch as it no longer contains either nerve-cells or nerve-fibres. A very occasional nerve-fibre may be found in these areas of gliosis.

It seems obvious from the structure of this tissue that it is quite capable of transmitting the pull which the contracting cicatrix must have exerted

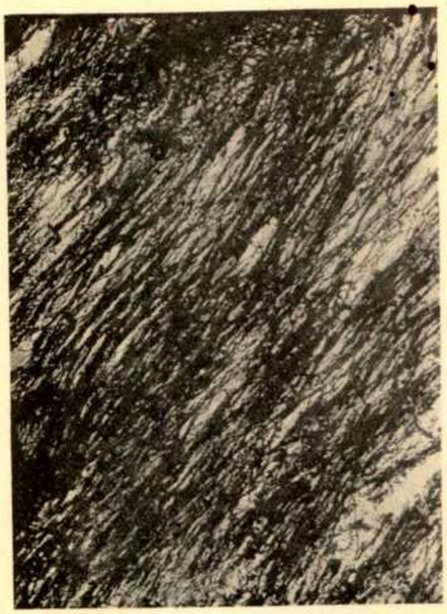


FIG. 6.—*Case* 1. Parallel neuroglia fibres oriented in the direction of the cicatricial pull. Silver carbonate astrocyte stain, Hortega.

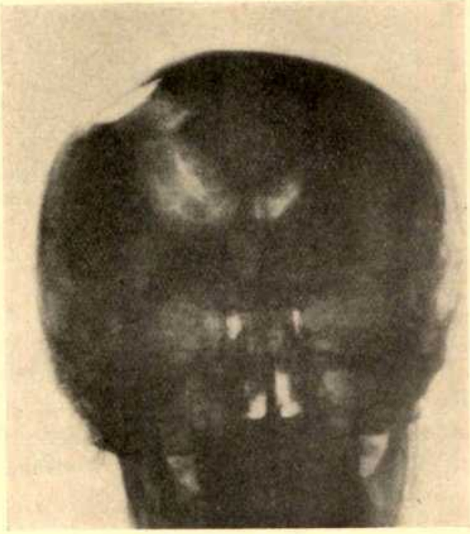


FIG. 7.—*Case* 2. Encephalogram (brow up), fourteen years after gunshot wound of right parietal region; shows cranial defect, the underlying brain cyst, enlargement of right lateral ventricle and pulling of all three ventricles in the direction of the defect.

upon the brain itself, as evidenced by the migration of the ventricles towards the side of the lesion.

Case 2.—The patient received a gunshot wound in the right parietal region in 1914, which was followed by hemiplegia of the extremities on the left side. The hemiplegia, which has only partially disappeared was followed in 1919 by Jacksonian epilepsy of parietal field type (see legend with fig. 8).

Encephalography in 1928 showed the right lateral ventricle to be considerably enlarged. The air entered a cyst just beneath the cranial defect which was due to the wound. Both lateral ventricles and the third ventricle were deviated across to the right side and the right ventricle upward toward the defect (fig. 7).

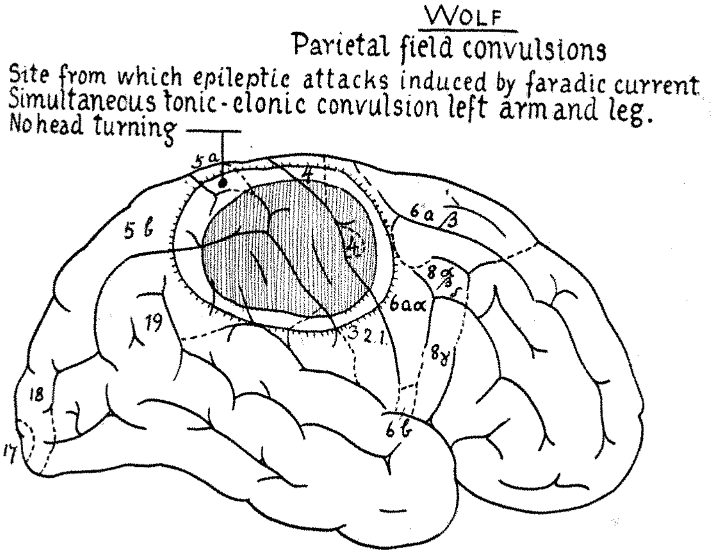

WOLF
Parietal field convulsions
Site from which epileptic attacks induced by faradic current
Simultaneous tonic-clonic convulsion left arm and leg.
No head turning
5a
4
5b
6aβ
4
8αβδ
6aα
19
3 2 1
8γ
18
6b
17

FIG. 8.—*Case* 2. Diagram from operative exposure. Jagged line indicates extent of cicatricectomy. Spontaneous attacks were preceded by sensory aura in the left leg or simultaneously in left leg and arm followed by head, eyes and body turning to left with tonic-clonic spasm of left arm and leg and rapid spread to extremities of right side.

Craniotomy in April, 1928.—Underneath the defect the dura was adherent to a cerebral scar; in the anterior part of the scar was a cyst. Posterior to this the tissue was hard and rather grey. Electrical stimulation near this indurated area produced a convulsion characterized by almost simultaneous movements of the left arm and leg, without head turning (fig. 8). A radical incision was carried out as indicated. Since the operation up till the present time (April, 1930) he had no more attacks.

The gross specimen showed dense adhesion of firm tissue to the under surface of the dura, and a large vessel near the point at which the stimulus had produced the convulsion.

Microscopical examination showed that the indurated areas contained strands of connective tissue and blood-vessels passing downward from the dura. Some of the vessels were surrounded by sclerotic rings of fibrous neuroglia. There was progressive destruction of tissue taking place as evidenced by pigment-laden cells around certain of the vessels, and also by isolated areas in which the microglia had undergone a partial alteration in the direction of compound granular corpuscles.

Case 3.—The patient received a gunshot wound in the right occipital region in 1914. A preliminary operation was done at once but the patient suffered from headaches and vertigo for some time, and he has had a left-sided homonomous hemianopsia since that time.

In 1916 epileptic seizures appeared, each attack being ushered in by a sensation of light in the left visual field. This was followed by turning of the eyes to the left, followed by turning of the head to the left and convulsive movements of the limbs of the left side, ending eventually in loss of consciousness.

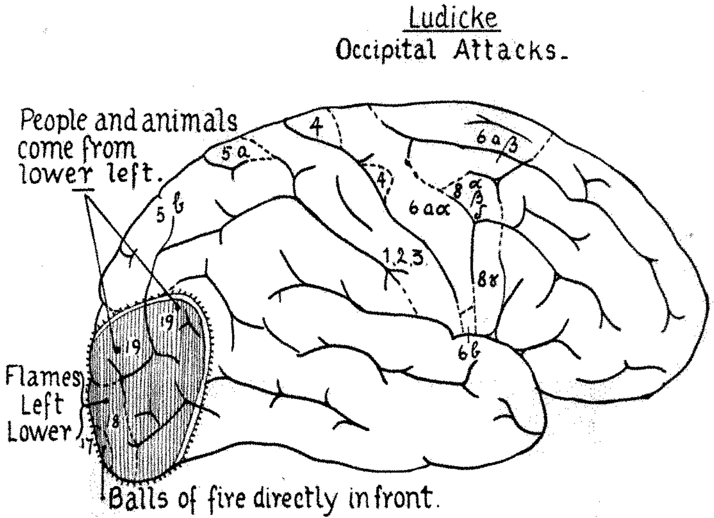


FIG. 9.—*Case* 3. Area of lesion seen at operation indicated by shading. Dots show points stimulated by electrode. The symptoms experienced by the patient following each stimulus are indicated on the chart.

Encephalography was carried out in 1927. This showed the posterior horn of the right lateral ventricle to be somewhat enlarged, to be displaced to the right and evidently to communicate with a cyst in the vicinity of the cranial defect. Both ventricles, even as far forward as the thalamus, were displaced somewhat to the right.

Occipital craniotomy was carried out in January, 1927. The dura was found to be densely attached to the cerebral cicatrix in the occipital lobe. Electrical stimulation of field 19 (see fig. 9) caused people and animals to be seen in the left field, and flames or balls of fire were produced by stimulation in field 18 nearer the occipital pole.

The whole area was radically excised; the epileptic seizures became less frequent and less intense but did not disappear entirely. One complicating factor in this case is the fact that the patient acquired syphilis in the year following the onset of his epilepsy.

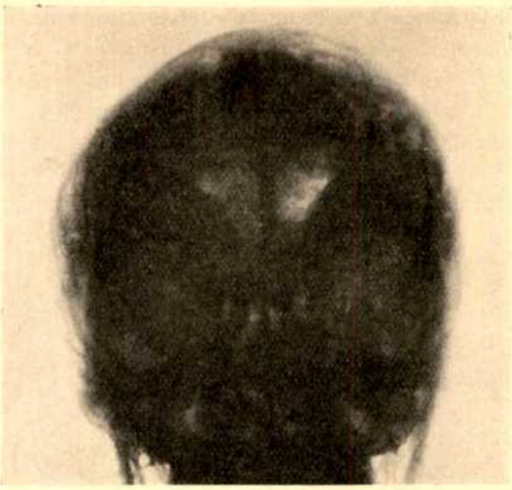


FIG. 10.—*Case* 4. Encephalogram (brow up) eleven years after shell wound of right frontal lobe. Lateral ventricles pulled to right and upwards towards the scar. The radiogram has been reversed in reproduction.

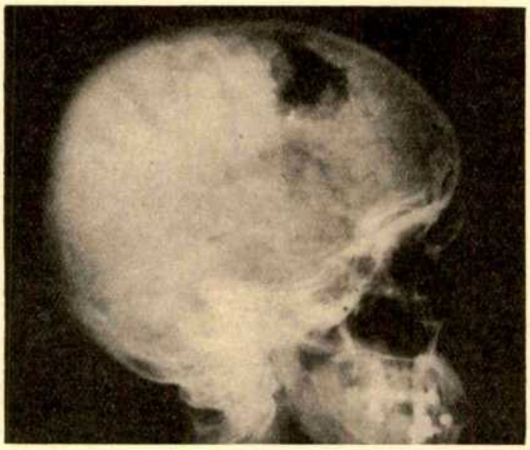


FIG. 11.—*Case* 4. Encephalogram (right side of head up) showing cranial defect with enlargement of anterior horn of the right lateral ventricle, and deflection upward of parts of both anterior horns.

In the excised cerebral cicatrix were two pieces of bone and a remarkable amount of connective tissue.

Case 4.—In 1914 the patient received a shell wound in the right frontal lobe. There was apparently no loss of consciousness and an immediate operation was performed. One year later the cranial defect was closed. At the end of four years, in 1918, the patient began to suffer from epileptic attacks which were of the type of those arising in the frontal adversive field. The eyes and head turned to the left without any sensory aura. This was followed by movements of both the left extremities.

Encephalography which was carried out in 1925 showed that the right lateral ventricle was somewhat larger than the left and was displaced upward and laterally. The third ventricle was displaced to the right and the left lateral ventricle seemed to be tipped, as though there had been a pull upward toward the cranial defect in the right upper frontal region (fig. 10). In the lateral view (fig. 11) the enlargement and upward deviation of the right lateral ventricle is easily seen.

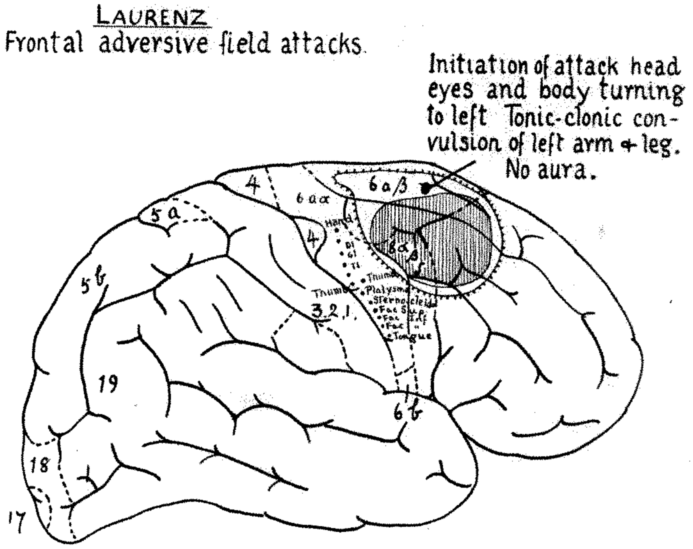

LAURENZ
Frontal adversive field attacks.
Initiation of attack head eyes and body turning to left Tonic-clonic convulsion of left arm + leg. No aura.
4
6aα
6aβ
5a
5b
Hand
4
DI
GI
TI
Thumb
Thumb
Platysma
Sterno cleid
Fac Sup.
Fac Inf
Fac "
Tongue
3,2,1.
6aα
β
19
6b
18
17

FIG. 12.—*Case* 4. Lesion as seen at operation. Motor response to galvanic stimulation indicated by small dots. Point at which convulsion was induced by faradic stimulation indicated by large dot.

Frontal craniotomy was carried out in 1925. A dense adhesion between the dura and cerebral cicatrix was found. Electrical stimulation of the brain at the border of the cicatrix (fig. 12) initiated an attack which was quite typical of those from which the patient suffered ordinarily.

The operative recovery was satisfactory, and during the three years which followed the operation there were no further convulsions.

The excised tissue contained yellowish grey gelatinoid material as is usual in these cicatrices. Two bits of shell were found embedded in the tissue. Histologically there was a large amount of gliosis and remarkable parallelism of the glia fibres. There was a very well-developed vascular plexus entering the scar (fig. 13).

Case 5.—In 1916 the patient received a gunshot wound in the parietal region near the vertex, a little more on the left than the right. An immediate operation was carried out. There followed a bilateral spastic paresis, more marked on the left side and associated with sensory disturbances of both legs.

In 1923 he began to have epileptic seizures typical of those arising in the right parietal adversive field. The head and eyes turned towards the left and then suddenly simultaneous movements appeared in the left arm and leg, followed quickly by the right leg.

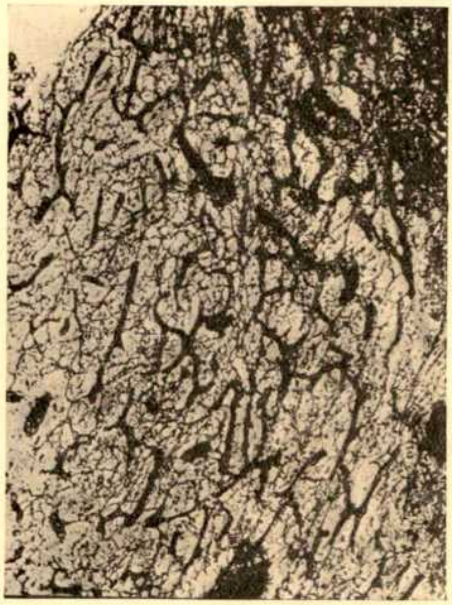


FIG. 13.—*Case* 4. Plexus of vessels and collagen fibres entering brain from overlying cicatrix. Silver carbonate connective tissue stain.

Encephalography showed some enlargement of the lateral ventricles and an upward deviation of the right side.

Parietal craniotomy was carried out and a large meningocerebral cicatrix found. The operation was carried out in two stages. At the first operation during the dissection of the scalp free from the dura, several typical convulsions were produced apparently as a result of the manipulation of the scar.

At the second stage of the operation electrical stimulation of the brain in the vicinity of the scar produced a typical attack. A wide excision was carried out as indicated (fig. 14). The excised tissue showed the usual type of contracting cicatrix. During the four years which have elapsed since operation the patient has been completely free from any attacks.

Case 6.—The patient gave an obvious history of birth injury followed by right-sided hemiplegia which gradually improved during boyhood. There was normal mental development up to the age of 12, after which time he was somewhat retarded. At 14 he began to suffer from epileptic seizures which began

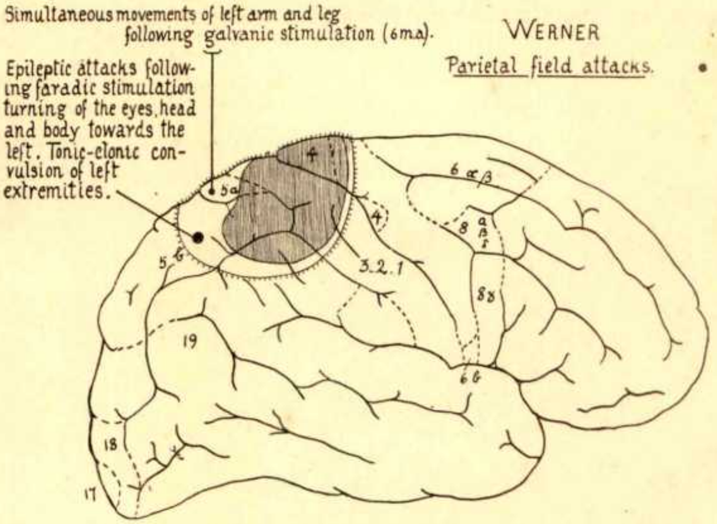

Simultaneous movements of left arm and leg following galvanic stimulation (6ma).
WERNER
Parietal field attacks.
Epileptic attacks following faradic stimulation turning of the eyes, head and body towards the left. Tonic-clonic convulsion of left extremities.
4
5a
4
6 α β
8 α β γ
5 6
3.2.1
8 δ
19
6 b
18
17

FIG. 14.—*Case* 5. Location of lesion and extent of removal.

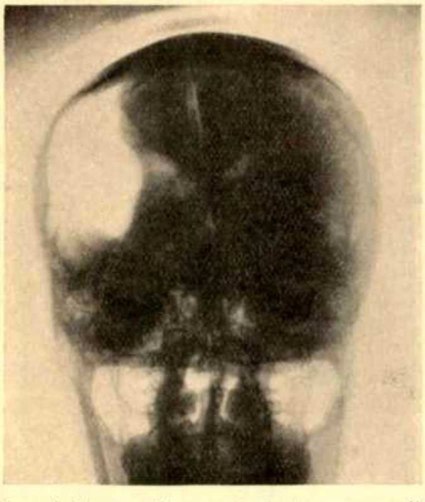


FIG. 15.—*Case* 6. Encephalogram (brow up) nineteen years after birth injury. Cyst of left hemisphere. The radiogram has been reversed in reproduction.

with movements of the right arm and leg, and simultaneous turning of the head and eyes to the right, followed by a generalized convulsion.

At the age of 19 encephalography showed a large cyst in the left cerebral hemisphere and some enlargement of the ventricle on that side (fig. 15).

Craniotomy exposed two large cysts close together. Electrical stimulation between the cysts (fig. 16) produced a typical convulsion. Both cysts were excised together with an indurated intravening area of cicatrix (fig. 17). The tissue of this scar presented a curious appearance (fig. 18), being made up for the most part of strands. These strands were composed of neuroglia cells with long parallel fibres, each strand being surrounded by a coating of collagen. The arrangement resembled that seen in peripheral nerves.

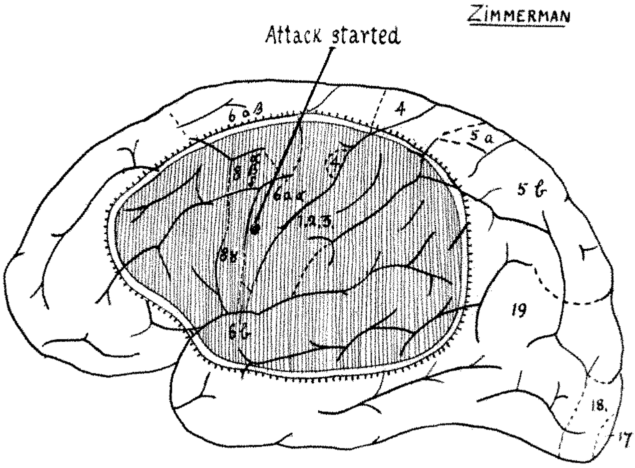


FIG. 16.—*Case* 6. Extent of lesion as seen at operation shown by shading. Extent of removal indicated by jagged line. Faradic stimulation at large dot between cysts inaugurated an attack.

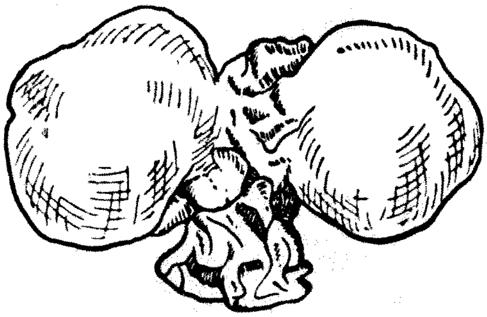


FIG. 17.—*Case* 6. Sketch of excised tissue after formalin fixation showing the two cysts.

The patient had been entirely free from epileptic seizures when last heard from three years after the operation.

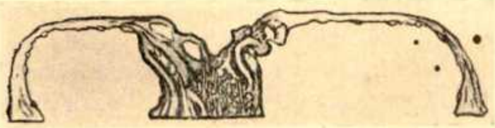


FIG. 18.—*Case* 6. Cross section of the two cysts and the intervening cicatrix. Note the fibrous strands.

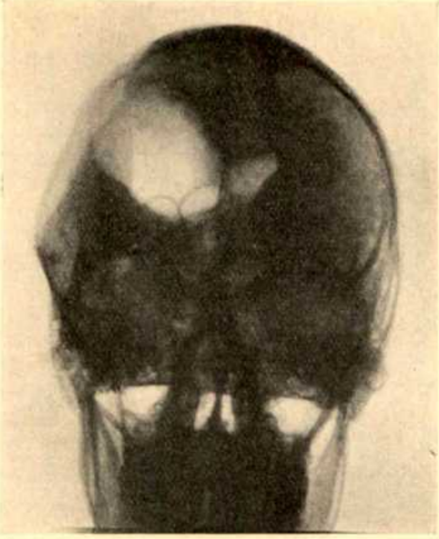


FIG. 19.—*Case* 7. Encephalogram (brow up) nineteen years after birth injury, showing enormous enlargement of right lateral ventricle and some pulling of the third ventricle across toward the right side.

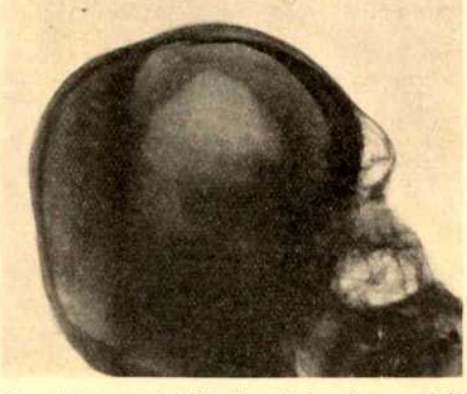


FIG. 20.—*Case* 7. Encephalogram (right side up) showing cranial defect from previous exploration and enlargement of anterior horn of right lateral ventricle.

Case 7.—This is a second case of cerebral birth injury followed this time by left-sided hemiparesis. At the age of 9 he began to suffer from epileptic attacks typical of those arising in the right frontal adversive field. The head and eyes turned to the opposite side followed by convulsive movements of the opposite extremities. The following year an opening was made in the bone over the right frontal area without entering the dura. This was without effect on the epilepsy.

Encephalography in 1928, at the age of 19, showed enormous dilatation of the right lateral ventricle with some displacement of the third ventricle across to the right side (fig. 19). The enlargement was chiefly in the anterior end of the ventricle (fig. 20).

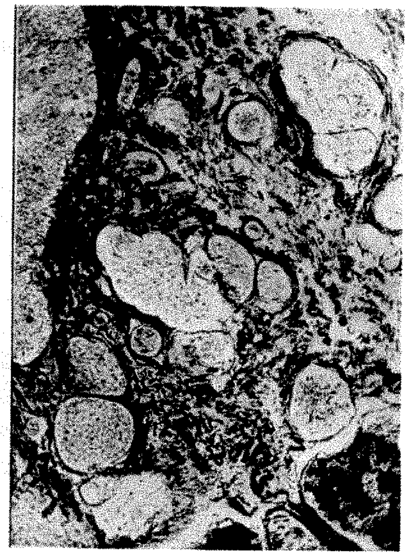


FIG. 21.—*Case* 7. Low-power photomicrograph of strands of cicatrix in cross section. Collagen makes a dark line about each. The dots within are neuroglial nuclei.

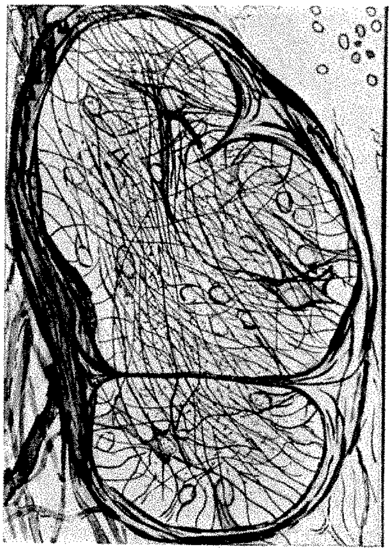


FIG. 22.—*Case* 7. High-power sketch of one of the strands seen in fig. 21. Some of the astrocytes can be seen to apply large processes to the collagen lining. The fine fibres are all neuroglial and arise from these cells. The dots indicate numerous such fibres cut across. Silver carbonate astrocyte stain, Hortega.

Craniotomy the same year demonstrated a dense adhesion between the dura and the brain scar. Dissection of the scar produced a typical attack. The lesion was excised, thus removing the lateral wall of the ventricle.

This excised tissue like that examined in the last case contained strands of glial tissue in which no nerve-fibres were to be found. The neuroglia cells were fibrous, containing many long, slender neuroglia fibres. These strands were coated with collagen and the neuroglia cells within were attached by numerous footplates to the under surface of the collagen covering. This is tissue capable of withstanding a considerable pull. These strands (fig. 21 and 22) were unlike any other type of pathological material. The tissue can hardly be called cerebral tissue in the strictest sense, inasmuch as there are no nerve-cells and no nerve-fibres in it, and although the tubes are composed entirely of neuroglia they have been coated over with collagen, just as nerve-fibres in other portions of the nervous system are invariably covered.

OPERATIVE TECHNIQUE.

The general preparation and pre-operative study are indicated in the outline of the above cases. Operation must be carried out under local anæsthesia. After electrical exploration radical excision is practised.

The removal should go deep enough to carry away all of the injured tissue and is best carried out by passing sutures deep down into the brain and tying them one by one so that the suture itself cuts through the cerebral tissue and procures hæmostasis of the blood-vessels in the pia arachnoid. The defect in the dura should be closed by the insertion of a piece of fascia. Operations that provide for the closure of the bone defect without removal of the scar can hope to accomplish nothing. Likewise dissection of the dura free from the scar and the interposition of an implant should only make matters worse, for no matter what the implant may be, it stimulates the formation of increased amounts of connective tissue. Only radical excision can remove the scar and relieve the abnormal physical strain. Anything less will serve only to increase the cicatrizing process.

There are minor differences in operative procedure as carried out by the two authors. In the neuro-surgical clinic at Breslau the bone is removed permanently over the area of operative exploration, while in Montreal the original procedure has been modified to the extent of replacing the bone flap. The important feature is that the removal is radical, clean, and directed toward the lesion responsible for the attacks.

DISCUSSION.

There were five additional cases included in the original report which will not be cited here; the ones already taken up being sufficient to serve as examples. These cases were selected because they illustrated certain aspects of the problem of traumatic epilepsy. Numerous similar cases could be added from the experience of each of the authors.

In each of the twelve cases studied there was displacement of one or all of the ventricles towards the side of the lesion. In most of the cases there was some degree of enlargement of the ventricle on the side of the lesion. In the two cases of birth injury the enlargement was enormous. That the local atrophy is not the cause of the deflection of the ventricles towards the site of the lesion is shown by the fact that the wandering of the ventricles is not greater in those cases where the atrophy is great. Likewise cases of cerebral thrombosis do not show this ventricular displacement and many cases with little or no enlargement of the lateral ventricle may show quite marked ventricular displacement. Instead of wandering of the ventricles the process is really brain-pull or ventricle-pull.

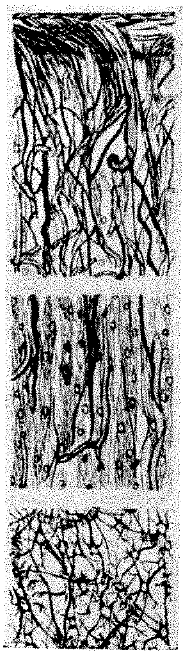


FIG. 23.—Schematic drawing of three levels in any meningo-cerebral cicatrix of long standing. Uppermost panel shows blood-vessels and bundles of collagen penetrating the brain beneath the meninges. Middle panel from area farther below surface shows intimate relationship of collagen strands and fine-fibred neuroglia, all parallel and pointing in the direction of the cicatricial pull. Lowermost panel from an area deeper in the brain shows the structure of astrocytes and blood-vessels which make up the vaso-astral framework and transmit the cicatricial pull.

Its seems evident that cicatricial contraction is responsible for the displacement of the ventricles in these human cases just as has already been demonstrated experimentally. Histological examination of this human material provides eloquent evidence of a long-continued cicatricial traction. There was always fibrous tissue, especially near the surface, and adhesion to the meninges (fig. 23). Thus connective tissue and an astonishingly rich plexus of vessels were invariably present in the scars, intermingled with fibrous astrocytes whose fibres were in general arranged in parallel and extended in the direction of the obvious traction, that is upward toward the cicatrix (fig. 23, middle panel). Deeper down in the brain (fig. 23, lowest panel) the astrocytes and blood-vessels still continue to form the only framework capable of withstanding tension, the vaso-astral framework [1].

In the areas of gliosis nerve-fibres are rare and nerve-cells still rarer. Occasionally localized areas are found in which there are groups of phagocytes containing pigment. Such patches are evidently in the vicinity of blood-vessels which have been shut off and they seem to indicate that the process of cerebral destruction is a long-continued one as they were present twelve and fourteen years after the initial wound. These areas recall the focal perivascular destruction described by Spielmeyer [3] in epilepsy of a different type.

The most extreme degree of progressive scarring is seen in the two cases of birth injury, both of which were of nineteen years standing. In these cases the process of connective tissue invasion and fibrillation of neuroglia had gone to such a point that there were tubes and sheets of neuroglia surrounded by connective tissue sheaths. Even where local atrophy and destruction had given rise to the presence of cysts there was always to be found also an area of grey, gelatinous fibrous tissue, the centre or the focus of concentric traction.

One further convincing evidence of the physical pull which these scars exert is the fact that in one of these cases reported here and in a number of others which we have observed, there was a definite pulling in of the scar which was noted as soon as the bone was removed and the edges of the adherent dura incised. The centre of the scar thus drew itself together, sucking the attached dura inward as much as 1½ cm. as soon as it was freed from the attachment to the overlying skull.

RELATIONSHIP OF CICATRICIAL CONTRACTION TO TRAUMATIC EPILEPSY.

An outstanding feature of all of these scars is the rich plexus of newly-formed vessels in and about the cicatrix. This vascular plexus anastomoses very freely with the large vessels which enter the scar from without. It also anastomoses freely with intracerebral vessels inasmuch as the surface of the dura continues to bleed after it is completely exposed and cut free from surrounding dura. We have already shown [1] also that experimentally this vascular plexus can be injected either by way of the external carotid artery or through the internal carotid.

During the years which follow the infliction of a brain wound there is evidently a progressive increase in the vascular elements of the scar and a progressive decrease in the nervous elements. Associated with these two changes is the steady cicatricial contraction which obviously takes place for an indefinite period.

Now if the stimulus for an epileptic seizure arises in the nervous elements one might expect the attack to begin shortly after the infliction of the wound when these elements are plentiful and undergoing progressive destruction. If, on the other hand, the vascular elements are responsible for the initiation of the process, epilepsy might well be expected to make its appearance later when the vascular plexus reaches its fullest development and nerve-fibres have largely vanished.

In the twelve cases reported, the time between the wound and the onset of convulsion varies between five months and fourteen years, the average period of immunity before the onset of attacks being five years and six months. The acute effect of the injury must have disappeared long before the end of the fifth year. There remains, however, one process progressive through all these years, and that is the cicatricial contraction which gradually draws one or both hemispheres toward the lesion.

We have shown that at operation the focal epileptic attacks may often be produced in two ways: either by electrical stimulation of the brain in the neighbourhood of the wound, or by gently pulling upon the adherent dura. This latter fact may be of considerable significance, for if increase of a pre-existing strain produces an attack it may well be that the pre-existing strain itself is an important factor in the ætiology of spontaneous convulsions.

As pointed out above, the blood-vessels form in one sense the woof of the contracting network. Traction, therefore, upon the vessels must be inevitable. The hypothesis at once suggests itself that a vaso-motor reflex secondary to this traction is responsible for the initiation of the convulsive seizures.

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THE ANTERIOR CEREBRAL ARTERY, AND ITS SYNDROMES.

BY MACDONALD CRITCHLEY.

COMPARATIVE ANATOMY.

THROUGHOUT the animal series the anterior cerebral artery has varied considerably in uniformity and has tended to become more complex with the mammalian ascent. Closely associated with the type of anterior cerebral artery has been the conformation of the forward portion of the circle of Willis.

The most primitive pattern is encountered amongst the fishes, amphibians, reptiles and birds. Here there is no real circle of Willis, as no anterior communicating artery occurs. The two anterior cerebral arteries are represented by a pair of small vessels lying parallel on the mesial aspects of the olfactory lobe. Hofmann [35] has shown that in the fish the anterior cerebral artery in its forward course sends small twigs to the under-aspect of the frontal lobe and terminates in the mesial aspect of the hemisphere in a series of small vessels. Although no anterior communicating artery is the rule, Schöbl [53] has described a ramus communicans in the salamander. In snakes, tortoises and crocodiles the anterior cerebral artery of each side may unite to form a common azygos artery from which arise the main vessels to the olfactory bulbs. Rathke proposed the name arteria ethmoidalis communis for this vessel.

Amongst birds the anterior cerebral artery is represented by a very small paired vessel having no communication with its fellow. The true ramus cranialis of the carotid artery is constituted by a large ethmoidal artery which passes forwards through the ethmoidal foramen.

Mammals.

In the giant ant-eater one encounters the primitive avian type, with small paired arteries and no ramus communicans; there is, therefore, no true circle of Willis.

The typical mammalian pattern consists in two short anterior cerebral arteries which converge and unite to form a median azygos vessel; this may or may not bifurcate later. There is no anterior communicating artery. The chief territory of the anterior cerebral artery and its branches is the forward portion of the rhinencephalon. Shellshear [60] has recently made a minute study of the morphology of the anterior cerebral artery in the spiny ant-eater. Here, the circle of Willis is completed in the usual mammalian fashion. The azygos

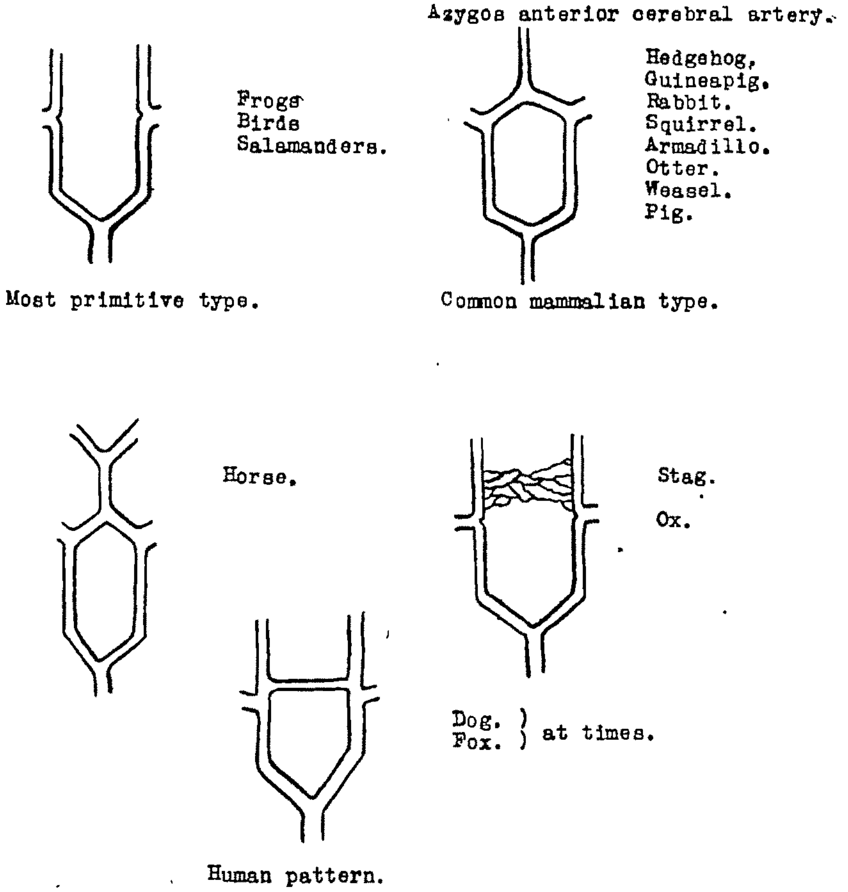

FIG. 1.—Schematic representation of the circle of Willis in animals lower than monkeys.

vessel lies in the median cleft of the brain between the two tubercula olfactoria, and terminates by dividing into a number of branches to the medial surface of the bulb and neopallium, including vessels to the anterior perforated spot, the postero-medial region of the tuberculum olfactorium and the area præcommissuralis; finally a large branch passes outwards to anastomose with a branch of the middle

Sylvian artery. In this way a vascular ring is formed around the tuberculum olfactorium. Shellshear identifies this particular branch with the so-called artery of Heubner in the human brain.

In mammals possessing a corpus callosum, the azygos anterior cerebral artery usually divides after a variable distance into two small "arteries of the corpus callosum" which run side by side over the dorsum of that structure.

The course of distribution of the anterior cerebral artery in the cat may be studied rather more closely, as typifying the usual lower mammalian arrangement. Shortly after the junction of the two arteries immediately below the genu of the corpus callosum, two vessels are given off, one to each hemisphere. The branch to the left cerebrum emerges before the one to the right side. The vessel ascends directly upwards in the vertical limb of the sulcus cruciatus, where it divides into anterior and posterior branches (see fig. 2). The anterior division proceeds to the motor and sensory areas, while the posterior branch turns backwards and then upwards over the most anterior portions of the sulcus splenialis to the parietal region. The azygos anterior cerebral artery now divides into two arteriæ corporis callosi which pass backwards in close apposition over the dorsum of the corpus callosum. Midway between the genu and the splenium, a second branch crosses the gyrus fornicatus, bends backwards for a short way in the sulcus splenialis and then, after making a second bend, runs upwards into the foremost extremity of the sulcus suprasplenialis. The terminal portion leaves the corpus callosum just anterior to the splenium and runs

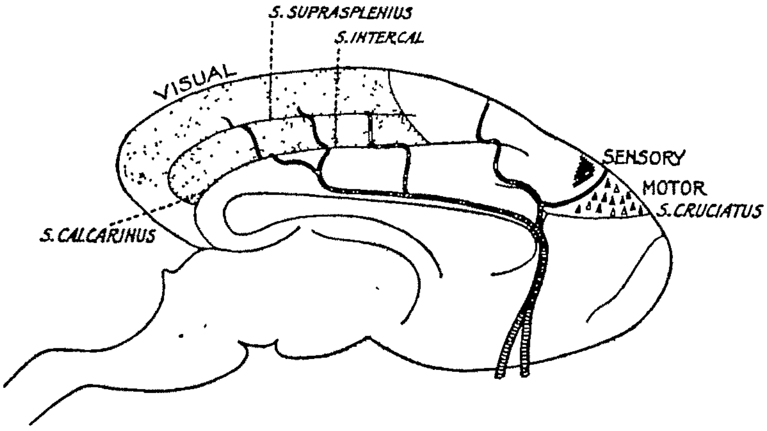

FIG. 2.—The anterior cerebral artery in the cat.

upwards and backwards. Before entering the sulcus splenialis it divides into anterior and posterior branches. These also run upwards parallel to each other and terminate in the mesial aspect of the visual area, in the gyrus suprasplenialis and the gyrus postsplenialis.

In the horse the unpaired portion of the anterior cerebral artery divides in the region of the genu into four terminal branches, two of which are large and two are small. The two smaller vessels, the arteriæ corporis callosi, run parallel over the genu and dorsum of the corpus callosum to terminate in the region of the splenium. The larger vessels are distributed to the mesial aspects of both hemispheres. Each runs in the sublimbic fissure, whence it gives off two large branches which cross the gyrus fornicatus, and after dipping deeply into the calloso-marginal gyrus, terminates in the superior border of the convex surface. (See fig. 3). The main trunk of the vessel leaves the sublimbic sulcus at about the middle of the corpus collosum and terminates by dividing within the depths of the calloso-marginal fissure into two vessels. A small arteriole arises from the point of angulation and passes backwards in the callosal sulcus. These two larger vessels represent the marginal artery.

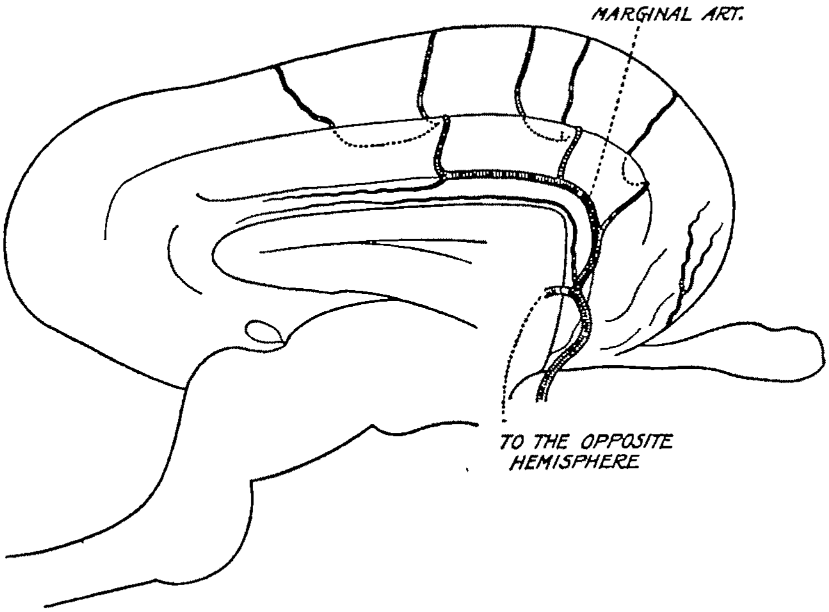

FIG. 3.—The anterior cerebral artery in the horse.

A still greater disproportion is seen in the brain of the calf, between the size of the arteries of the corpus callosum and the marginal vessels. In the particular specimen examined there was an anterior communicating artery connecting the two anterior cerebral arteries. Immediately in front of this was a second and finer anastomotic vessel. The anterior cerebral artery then divided into a fine artery of the corpus callosum, and a large marginal artery. The latter turned forwards in the mesial aspect of the frontal lobe and then bent back so as to enter the callosomarginal fissure. Immediately before entering this sulcus a large anterior branch is given off to end in the sulcus coronarius (see fig. 4).

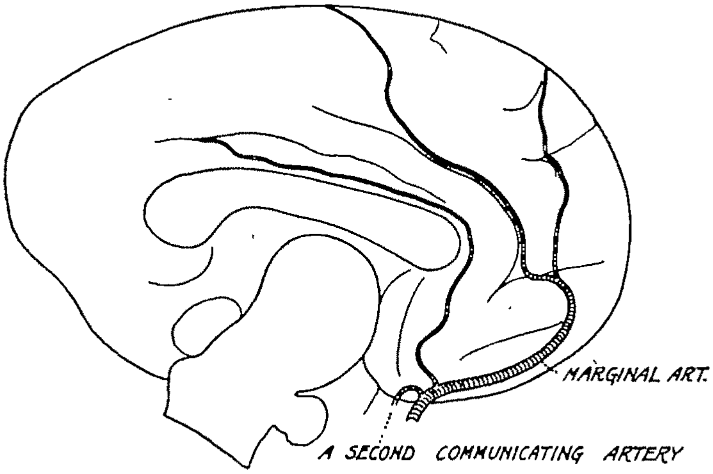

FIG. 4.—The anterior cerebral artery in the calf.

Amongst the lower monkeys (baboons, macacques, long-tailed monkeys) there is a great variability in the pattern of the anterior aspect of the circle of Willis and numerous transition forms are encountered between the mammalian and human types. Thus, in a series of thirty-two lower monkeys examined by Rothmann [52], a primitive mammalian type of anterior cerebral artery was found in twenty (i.e., an azygos vessel, and no anterior communicating artery); in five cases a small vascular loop occurred at the point of junction of the paired and unpaired vessels, and in one instance there was a double loop. In two cases the paired portion of the anterior cerebral artery was well developed on one side only; in another case the azygos vessel arose from the internal carotid artery. In only three instances was there any suggestion of a human pattern of an atypical type.

A more detailed study of the branches of the anterior cerebral artery in the baboon shows an obvious similarity with the human pattern (see fig. 5). Thus, the first branch passes horizontally forwards to supply the gyrus rectus. Immediately below the genu a large branch passes forwards and upwards to enter the deep calloso-marginal sulcus, whence it emerges to pass to the cortex as high as the supero-mesial border. It supplies the internal aspect of the frontal lobe as far posteriorly as the midfrontal sulcus. The third branch is given off just behind the genu; it runs parallel with the previous branch, enters the depths of calloso-marginal sulcus, and emerging thence passes to the uppermost part of the lateral surface. It supplies the area between the midfrontal sulcus and the fissure of Rolando. The fourth branch arises about the centre of the corpus callosum. It passes upward and slightly forwards, dipping deeply into the calloso-marginal fissure, and ends in the area surrounding the mesial prolongation of the fissure of Rolando. A fifth branch is given off at the junction of the posterior third with the anterior two-thirds of the corpus callosum; just before entering the calloso-marginal sulcus it gives off a posterior branch which communicates with the sixth branch. The main stem enters the calloso-marginal sulcus and emerges at a little distance anteriorly, whence it passes directly upwards to supply the post-central cortex. The sixth branch does not enter the calloso-marginal sulcus but turns back to run below and parallel with it as far as the precuneus. The terminal portion of the anterior cerebral artery turns abruptly up at the level of the splenium and then almost immediately changes direction so as to run

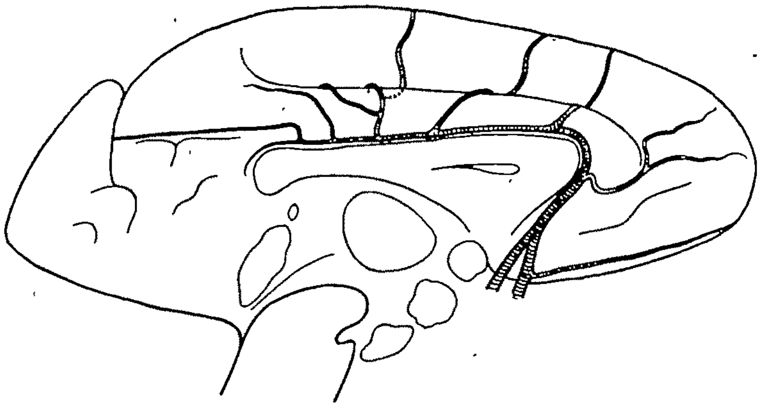

FIG. 5.—The anterior cerebral artery in the baboon.

backwards and slightly downwards to end in the parieto-occipital fissure. A tiny twig continues the direction of the main artery over the splenium and anastomoses with a twig from the posterior cerebral. These details of the branches of the anterior cerebral artery in the baboon agree in the main with the description given by Lesem [37]).

The arterial patterns in the higher apes show a greater tendency towards a human type than in the other mammals. In the chimpanzee, Rothmann found a typical human arrangement in one out of seven; in one there were two anterior cerebral arteries but no anterior communicating artery. In four the conformation was of the primitive mammalian type, whilst in one there were three anterior cerebral arteries with an arterial loop at the point of trifurcation. Grünbaum and Sherrington [31] discovered a human pattern in five out of six chimpanzees, while in one only was there an azygos anterior cerebral artery. In one chimpanzee brain, studied in great detail by Shellshear [61], the vessel was of the mammalian type. His work reveals a striking similarity in the distribution of the deep and superficial branches between the chimpanzee and the human brains. Professor Elliot Smith has very kindly permitted me to read the manuscript of Shellshear's paper.

No anterior communicating artery was found in either of the two orang brains examined by Bolk [16]. A characteristic human conformation existed in the brain of one orang examined by Grünbaum and Sherrington. In Rothmann's four cases no typical specimen was found, either of the human or of the mammalian type. In two, there was an asymmetry between the two sides; in one there were three anterior cerebral arteries, and in another there were numerous anastomoses between the two anterior cerebral arteries. Shellshear [58] has studied minutely the morphology of the cerebral blood-vessels in an orang brain. In this particular specimen, the circle of Willis was completed in the normal human fashion. The branches from the first part of the artery, that is from its origin to the anterior communicating vessel, supplied the anterior commissure, the corpus striatum lying in front of the anterior commissure, the olfactory tract, the mesial and lateral olfactory striæ, the tuberculum olfactorium, the corpus paraterminale and the proximal part of the gyrus cinguli. One branch from this region was conspicuous on account of its size; it probably supplied the caudate nucleus. Branches from the second part were purely cortical; the first, corresponding with the medial orbital branch in man, supplied the area præfrontalis; the second branch was called the anterior medial frontal and was distributed to the area frontopolaris. The third branch—which is often associated with the second—supplied the anterior frontal area of Elliot Smith. The fourth and fifth branches were termed the intermediate and posterior medial frontal respectively, and irrigated the superior frontal and paracentral gyri. Other twigs supplied the posterior part of the gyrus cinguli and the area parasplenialis. The anterior cerebral artery terminated in the parieto-occipital fissure.

The brains of two gorillas in Rothmann's series both showed a typical human formation.

Out of four brains of gibbons, Rothmann found a mammalian pattern three times. In a fourth there were two anterior cerebral arteries, but the anterior communicating artery was replaced by a large vascular knot.

ANATOMY OF THE ANTERIOR CEREBRAL ARTERY IN MAN.

In the human anterior cerebral artery a still greater degree of complexity is reached, although the main conformation resembles closely that seen in the higher apes.

Arising as one of the two terminal branches of the internal carotid, the anterior cerebral artery first passes forwards and inwards across the anterior aspect of the anterior perforated spot. It crosses between the tuberculum olfactorium and the optic nerve and so comes to lie at the margin bounding the mesial and orbital surfaces of the hemisphere. At this point the two arteries are connected by the short anterior communicating artery. The anterior cerebral artery then abruptly changes its direction and turns upwards and slightly forwards so as to reach the genu of the corpus callosum. It now follows the epicallosal sulcus and lies along the body of the corpus callosum as far as the junction of the posterior fifth with the anterior four-fifths. In this way it courses forwards, then upwards, backwards and slightly downwards, and finally pursues an almost horizontal course. The artery terminates by leaving the epicallosal sulcus, and passing upwards and backwards obliquely across the parietal lobe, ends either in the quadrate lobe or in the parieto-occipital fissure. Although the two anterior cerebral arteries lie in close apposition throughout their courses there is, in the majority of cases, no intercommunication after the anterior communicating artery.

The branches of the anterior cerebral artery may be classified as follows:—

(1) Basal (arising from the artery as it crosses the anterior perforated spot).

(2) The anterior communicating artery.

(3) The branches from the convexity.

(4) The branches from the concave aspect of the arterial course.

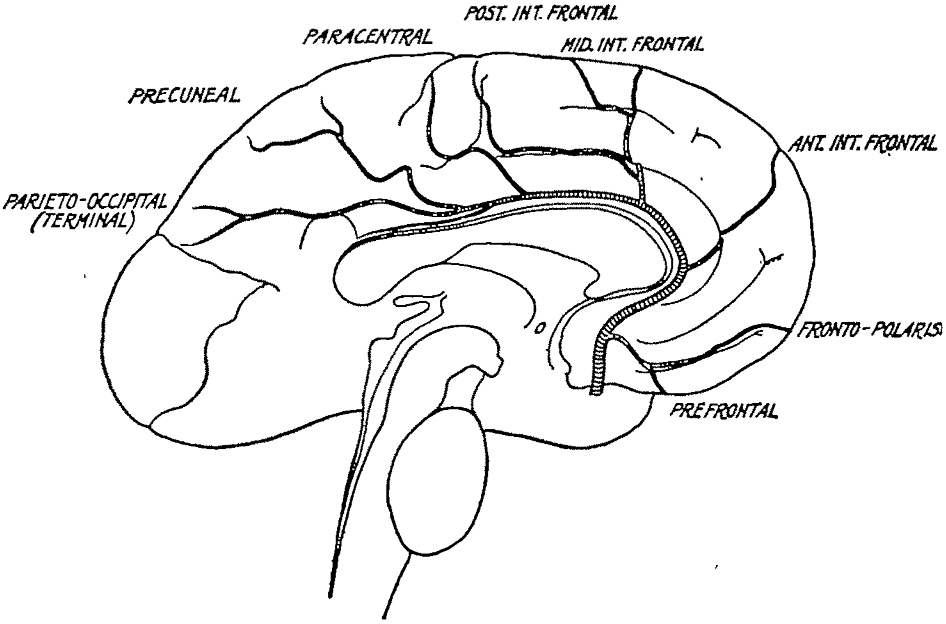

FIG. 6.—The anterior cerebral artery in man.

(*a*) *The basal branches.*—Although most French writers have minimized the importance of these vessels, the work of Heubner [33], which has been abundantly confirmed by others, illustrates their constancy and importance. According to the French school, the fine basal branches pierce the anterior perforated spot to supply the head of the caudate nucleus, but the basal ganglia and converging motor pathways are said to receive no supply from the anterior cerebral artery.

The fine basal branches, usually three or four in number, pass immediately upwards, parallel with one or two similar vessels from the region of the bifurcation of the internal carotid, and enter the anterior perforated spot through the most anterior row of apertures. They are distributed to the head of the caudate nucleus, and in particular to its anterior-inferior portion. At times the whole of its head may be so supplied.

One of the basal perforating branches of the anterior cerebral artery is important, however, on account of its size, its course and its distribution. This vessel—the recurrent artery, or the artery of Heubner [1]—emerges from the superior surface of the anterior cerebral artery, sometimes in the most mesial portion of the anterior perforated spot, sometimes at the lateral end. It may occasionally arise from the internal carotid at its bifurcation, or even from the middle cerebral. I have also seen it spring from the anterior cerebral artery after the emergence of the anterior communicating artery. According to Aitken [2], however, it arises in 80 per cent. of cases from the basal portion of the anterior cerebral artery. This vessel passes first downwards, and then almost immediately turns outwards and backwards towards the lateral extremity of the anterior perforated spot, which it pierces either as a single or as a double vessel. Before entering the substance of the brain it may occasionally send off a fine twig to the tuberculum olfactorium and the proximal portion of the olfactory peduncle. Within the brain it passes upwards and outwards, branching into three main stems, and ends in the anterior part of the caudate, the anterior third of the putamen, the tip of the outer segment of the globus pallidus, and the anterior limb of the internal capsule (see figs. 7, 8, 9, 10 and 11).

Another of the basal arteries, according to Aitken, constantly enters the anterior perforated spot through a large, centrally placed aperture and is distributed to the globus pallidus only.

(*b*) *The anterior communicating artery* is a short vessel (about 4 mm. in length) connecting the anterior cerebral arteries of both sides. It passes horizontally backwards, lying immediately above the optic nerves and in front of the chiasma. In man there are no branches, although when present in dogs it may send fine twigs to the stalk and the anterior lobe of the pituitary. (Dandy and Goetsch [20].)

(*c*) *The branches from the convexity* are the largest and most important.

These are variable in their mode of origin and two or three may issue from a common stem. There is a striking lack of uniformity in nomenclature, particularly on account of the survival of Duret's original terminology. Duret [21] described one chief branch which he named

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[1] The artery is named after Heubner, who, in 1874, described a vessel emerging from the interior cerebral artery which supplied the forelimb of the inner capsule, as well as the most internal and the middle lobe of the lenticular nucleus. Despite this work and the later researches of Beevor, Aitken and others, the French have continued to ignore its existence and to associate themselves with the original findings of Duret.

"the internal and inferior frontal artery," and he stated that the anterior cerebral artery terminated by dividing into three vessels, namely, an "internal and anterior frontal artery," the "internal and medial frontal artery," and the "internal and posterior frontal artery."

In this paper the terminology employed by Shellshear is largely adopted, with one or two modifications. The branches may be described as follows:—

(1) *The prefrontal branch* (syn., the orbital artery of Foix; the internal orbital artery).—This vessel arises almost immediately after the emergence of the anterior communicating artery. It bends downwards to the orbital surface of the frontal lobe and crosses obliquely the gyrus rectus. Here it frequently divides into two branches which pass dorsal to the olfactory peduncle, at the junctions of the anterior one-third and posterior two-thirds, and the anterior two-thirds and posterior one-third respectively. The prefrontal artery supplies the medial aspect of the frontal lobe below the sulcus subrostralis, the gyrus rectus, the olfactory peduncle and lobe, and the internal orbital convolution; it reaches as far forwards as the tip of the pole. Its territory corresponds closely with the *area præfrontalis* of Elliot Smith, or Brodmann's area, No. 11.

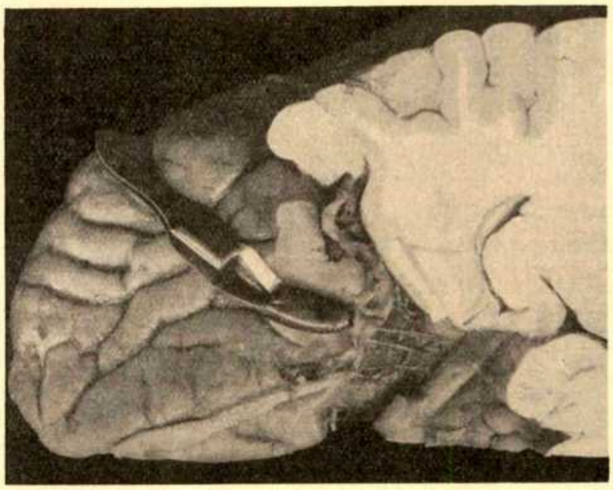

FIG. 7.—The anterior perforated spot of the left hemisphere of the human brain. The internal carotid artery has been turned forwards to display the first parts of the anterior and middle cerebral arteries. Three perforating branches of the anterior cerebral artery are seen passing backwards to enter the perforated spot. Heubner's artery runs transversely outwards above the perforating branches, and after dividing into two, enters the brain at the lateral extremity of the perforated spot. See also fig. 8.

Not infrequently the prefrontal artery arises as a branch of the frontopolaris artery.

(2) The *frontopolaris branch* (syn., the prefrontal artery of Foix; the internal anterior-frontal artery of Duret; the internal frontal artery of Lesem).—This vessel arises midway between the inferior border of the mesial surface of the hemisphere and the genu of the corpus callosum. The artery passes slightly downwards at first and then horizontally, lying in the sulcus rostralis. It terminates in the tip of the frontal pole where it supplies the most anterior portion of the superior frontal gyrus. This vessel possesses the most direct course of all the branches of the anterior cerebral artery. The subcortical territory of this vessel, as revealed by a horizontal section through the frontal pole, consists in a rectangular area measuring 2½ by 3 cm., bounded anteriorly by the cortex of the frontal pole, intermediately by the cortex of the mesial surface, and posteriorly by the tip of the anterior horn of the lateral ventricle.

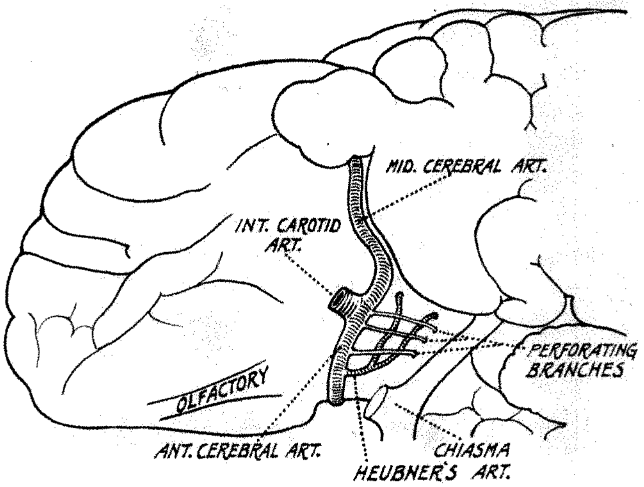

FIG. 8.—The vessels to the anterior perforated spot depicted semi-diagrammatically.

In man its territory corresponds with the *area frontopolaris* of Elliot Smith or the medial aspect of Brodmann's field No. 10.

(3) The *anterior internal frontal branch*. This branch emerges at the level of the genu. It passes forwards and upwards across the gyrus cingulus, to enter the depths of the calloso-marginal gyrus and terminate in the convex surface of the brain in the middle portion of the superior frontal convolution. It supplies the mesial portion of Brodmann's field No. 9 or the *area frontalis granularis*.

(4) The *middle internal frontal* arises at the level of the body of the corpus callosum and passes upwards to enter the depths of the calloso-marginal gyrus. After making a loop it emerges and passes up and slightly backwards. It frequently bifurcates before entering the convexity of the cerebrum, where it ends in the upper or posterior end of the superior frontal gyrus. The territory corresponds with the mesial portion of Brodmann's field No. 8, or the *area frontalis intermedia*.

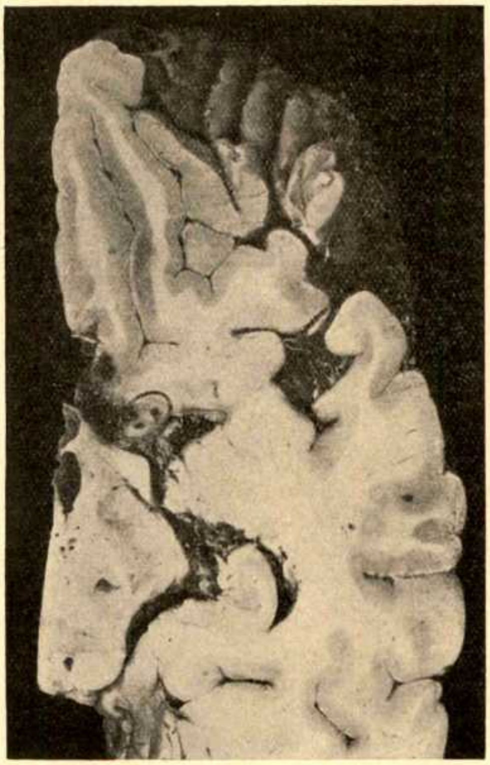

FIG. 9.

(5) The *posterior internal frontal branch* often emerges from a point just behind the former artery and runs upwards to the calloso-marginal sulcus. It then passes backwards in this fissure for a distance of 1 to 1·5 cm., when it again turns upwards, and ends in the uppermost limit of the precentral fissure. The area of its supply is roughly the medial aspect of Brodmann's field No. 6, or the *area frontalis agranularis*.

The three internal frontal arteries frequently do not leave the anterior cerebral artery by three stems, but may be combined; thus the anterior and middle may emerge from a common stem, or the posterior internal frontal may arise as a branch of the middle internal frontal. A particularly common mode of origin is for a vessel to leave the main trunk of the anterior cerebral artery at the level of the genu and to run forwards as far as the calloso-marginal fissure. Here, the vessel makes a right-angle bend and passes backwards in the depths of this fissure for a distance of 3 to 5 cm. It then makes a second bend at a right-angle

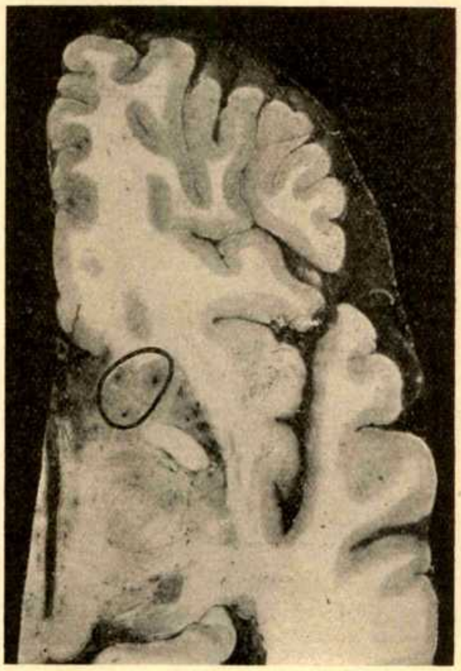

FIG. 10.

and crosses the marginal gyrus to reach the superior frontal convolution. In its course it gives off one, two or three branches; this vessel—known as the *calloso-marginal branch*—represents the fusion of two or more internal frontal arteries, including at times the paracentral artery. The calloso-marginal branch is probably the homologue of the marginal artery of the horse and cow; it is interesting to note how the disproportion which exists in these animals between the arteriæ corporis callosi and the marginal artery, is not encountered in man, owing to the relative greater importance of the corpus callosum.

At times all three frontal branches may arise as trifurcations of a single artery.

(6) The *paracentral artery* arises from a point about the middle of the corpus callosum and passes backwards and upwards to run for a short way in the calloso-marginal gyrus. It then changes its course again to run vertically upwards, ending in the substance of the paracentral lobule. In rare cases, this branch is actually the terminal portion of the anterior cerebral artery.

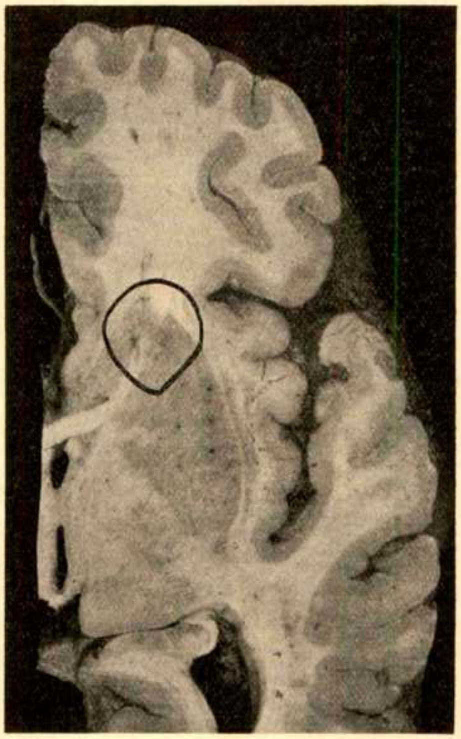

FIG. 11.

FIGS. 9, 10 and 11.—Dissections of the base of the brain to demonstrate the course and distribution of Heubner's artery. The vessel enters the brain in two divisions which later become three; they are distributed to the head of the caudate nucleus, the most anterior portion of the internal capsule and the head of the putamen.

(7) Occasionally, one, or even two, slender branches leave the anterior cerebral artery immediately behind the paracentral artery, and pass directly upwards to terminate in the post-central cortex and superior parietal convolution. These vessels may be termed the *superior parietal arteries.*

(8) The *precuneal branch* in many cases constitutes the terminal portion of the main trunk of the anterior cerebral artery. It leaves the corpus callosum at the point of junction of the posterior one-fifth and anterior four-fifths, and courses obliquely backwards and upwards across the parietal lobe to end in the quadrate lobule. Beevor [11] [12] found this mode of termination of the anterior cerebral artery in twenty-one of his series of forty-eight cases. Its territory corresponds with the mesial portion of Brodmann's field No. 7, or the *area parietalis superior*.

(9) In many instances (nineteen out of forty-eight: Beevor) the anterior cerebral artery ends as the *parietal-occipital branch.* In this case it leaves the dorsum of the corpus callosum immediately posterior to the precuneal artery and runs horizontally backwards to end in the parieto-occipital fissure.

In a single brain, the anterior cerebral artery of one side may end as a precuneal artery, and in the opposite hemisphere as a parieto-occipital artery.

(*d*) *Branches from the concavity.*—These include numerous short twigs to the genu and body of the corpus callosum. Some of them penetrate and supply the septum pellucidum, part of the anterior commissure and the anterior pillars of the fornix.

One longer but very delicate vessel (the *posterior pericallosal artery*) emerges from the under surface of the anterior cerebral artery between the points of origin of the paracentral and precuneal arteries. It passes backwards in the fissure of the corpus callosum, lying immediately under the main trunk of the anterior cerebral artery, and when this latter has left the fissure to form the parieto-occipital artery it continues along the body of the corpus callosum to unite, over the splenium, with a branch of the posterior cerebral artery.

The curved and backward sweeping course of the anterior cerebral artery and its branches is striking. French writers describe two concentric vascular semicircles: an inner one formed by the main trunk of the anterior cerebral artery and its continuation—the posterior pericallosal; and an outer, interrupted one, formed by the various branches in their passage along the calloso-marginal sulcus. The former is termed the "démi-cercle péricalleux" and the latter the "démi-cercle calloso-marginal."

The depth to which the branches penetrate the calloso-marginal sulcus has already been mentioned, although this feature is not so striking as in the brain of certain of the apes, e.g., the baboon.

Skiagraphy of the brain after the injection of a radio-opaque fluid as employed by Temple Fay [25] demonstrates this looping very clearly. Fay remarked that his negatives illustrate a striking difference in the territory of the anterior cerebral artery and of the other vessels; in the former, there were numerous swing-like loops drooping downward from the cortex into the depths of the convolutions towards the anterior horn of the lateral ventricle.

THE TERRITORY OF THE ANTERIOR CEREBRAL ARTERY.

One may indicate briefly the territory supplied by the anterior cerebral artery as follows:—

The whole of the mesial surface of the frontal and parietal lobes. The most posterior limit is variable; it usually reaches to the centre of the quadrate lobule, but at times it extends back as far as the parieto-occipital fissure; the most anterior limit is the post-central sulcus.

The white matter immediately subjoining the above area extending laterally into the hemisphere for a distance of about 2½ cm. A series of sagittal sections through a brain in which arteries have been injected shows that at a distance of 1 to 2 cm. from the mesial surface the most anterior wedge is supplied by the anterior cerebral artery, but there is an island in the centre corresponding with the supply of the perforating branches of the Sylvian. A section 4 cm. from the great longitudinal fissure reveals a reversal of the previous situation; the main area is supplied by the Sylvian, but an islet of anterior cerebral territory remains in the centre corresponding with the distribution of Heubner's artery.

On the orbital surface of the frontal lobe, the territory reaches laterally from the midline as far as the external limit of the internal orbital convolution.

The genu and anterior four-fifths of the corpus callosum.

The septum lucidum, the upper portion of the anterior pillars of the fornix and the medial part of the anterior commissure.

The inferior aspect of the anterior part of the head of the caudate nucleus; the anterior portion of the two outer segments of the lenticular nucleus, and the anterior half of the forelimb of the internal capsule.

ABNORMALITIES IN THE MORPHOLOGY OF THE HUMAN ANTERIOR CEREBRAL ARTERY.

In view of the changes which the anterior cerebral artery have undergone in the course of its acquisition of the human morphological pattern, it is not surprising to find occasional abnormalities in its conformation. Studies of the arterial patterns in the brain, carried out in a large series of cases, have demonstrated the frequency of such deviations. Thus, in his series of 200 cases, Windle [66] found anomalies in the anterior communicating artery in 41, and in the anterior cerebral artery in 19. Fawcett and Blatchford [24] found abnormalities in the region of the anterior cerebral artery in 26 cases out of 700. It has been suggested that abnormalities of this artery occur with some frequency in the brains of the insane or amongst criminals. Wyrubow [68], for example, saw unusual forms in 22·3 per cent. of 112 brains from asylum inmates, while Parnisetti [50] found abnormalities of this artery in 34·5 per cent. cases in a series of 87 criminal brains. Amongst fœtal brains (from seven months to term) abnormalities were present, according to Lesem, in 28 out of 32 (or 87·5 per cent.).

As already mentioned, variability in mode of branching occurs relatively often, and anomalies of this order have not been included in the above statistics. Amongst these anomalies may be mentioned the emergence of certain of the frontal branches from a common trunk. Thus it is not uncommon to find the frontopolaris issuing as a branch of the anterior-internal frontal; or the anterior, medial and posterior frontal emerging from a common stem. Any combination of adjacent arteries may be encountered. Under the term "bifurcation précoce," Foix and Hillemand [27] describe the junction of the frontopolaris with the three internal-frontal arteries into a common stem which leaves the main anterior cerebral trunk at the inferior border of the frontal lobe.

The presence of one or two fine branches to the superior portion of the parietal lobe has already been noted.

Variability in the site of origin of Heubner's artery has been a common finding. Posteriorly the artery may arise as a branch of the Sylvian or of the internal carotid, while the most anterior limit is the trunk of the anterior cerebral artery, after the emergence of the anterior communicating artery.

One of the most interesting anomalies consists in the presence of a third or median anterior cerebral artery arising from the anterior communicating artery which courses upwards and backwards over the dorsum of the corpus callosum. This vessel is also known at times as the *arteria termatica* of Wilder. According to Blackburn [13] [14], it frequently divides opposite the paracentral lobule into four large equal branches, which go to the paracentral and precuneal lobules of both sides. In such cases the anterior cerebral arteries proper are abnormally small and supply the anterior aspects of the medial surfaces of the hemispheres. The frequency with which a median anterior cerebral artery occurs is doubtful, owing to the variable statistics. Windle found it nine times out of 200 brains (4·5 per cent.); Parnisetti 7 times in a series of 87 brains of criminals (8 per cent.); Lesem 4 times in 32 fœtal brains (12·5 per cent.); Fawcett and Blatchford 23 times out of 700 brains (3·3 per cent.), and Blackburn 42 out of 400 cases (10·5 per cent.) Wyrubow reported the finding of a third anterior cerebral artery as "frequent" in his series of 112 brains from insane patients.

A much rarer anomaly is the presence of a primitive mammalian pattern, with a single azygos artery, and no anterior communicating vessel. Although Lesem found this type of artery 22 times among his 32 fœtal brains (68·75 per cent.), other observers have noted it as a rarity. It was reported by Wyrubow in his series of brains of the insane; Windle described it in 8 cases (4 per cent.).

More commonly, there may be an asymmetry in calibre between the two anterior cerebral arteries so that the vessel of one side supplies both hemispheres, sometimes by way of an hypertrophied anterior communicating artery, at other times by means of other connecting vascular channels. Or the anterior cerebral artery of one side may duplicate itself near its origin, and send one branch to the opposite hemisphere. A deformity of this type was described in 1879 by Ewart [23]. Sometimes this bifurcation occurs only after the artery has reached the dorsum of the corpus callosum (see Case 7). The first mentioned anomaly may appear, not only as a congenital morphological error, but also as the result of arterial disease. Thus, in the case of a female patient, aged 50, suffering from cerebral arteriosclerosis, the anterior cerebral artery of one side was so small in its course across the anterior perforated space as to be incapable of maintaining an adequate circulation; the opposite anterior cerebral artery therefore supplied both hemispheres by way of a large anterior communicating artery.[1]

Doubling or trebling of the anterior communicating artery is not very uncommon, and was described in 1868 by Henle [32], and eleven years later by Ewart. It also occurred in 12 of Parnisetti's 87 cases, and 15 of Windle's 200 cases. Other such cases have been reported by Incoronato, Barbieri [5], Spitzka [62], Weir Mitchell [47], Godinov [28], and others. Barkow [6] [7] has described an actual vascular plexus connecting the two anterior cerebral arteries. Sometimes the anterior communicating artery is abnormal in size and calibre; thus it may be unusually short (Weber [64]; Barbieri) or unusually large (Barbieri). In one case the anterior communicating artery was found to be impervious (Barbieri). Godinov has reported that the anterior communicating artery was V-shaped in 13 per cent., N-shaped in 4 per cent., and H-shaped in 3 per cent. of his series of brains.

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[1] An almost identical phenomenon was described by Barbieri in 1867 in his fourteenth case. Heubner has given a similar illustration on p. 197 of his monograph. Other analogous cases have been reported by Rendall (1879) [51], Beaumonoir (1886) [10], and by Beadles (1907) [9] who found such a specimen in the Museum of the Royal College of Surgeons No. 3795 I).

The anterior communicating artery is very occasionally absent; then the conformation of the anterior group of cerebral arteries recalls the primitive avian pattern (Barbieri, Spitzka). In a peculiar case quoted by Incoronato, there was no anterior communicating artery, but a circle of Willis was formed by the direct union of the two internal carotid arteries. The anterior cerebral vessels here formed a large quadrate lacuna or sinus before they separated.

Looping of the main trunk of the anterior cerebral artery is an unusual anomaly which has been reported by Shellshear in the brain of an orang-utan [58].

The Functional Significance of the Anterior Cerebral Artery.

We owe to Hilton [34] not only the conception of the constancy of arterial distribution, but also the hypothesis that the arteries are intimately associated with a definite physiological function. He quotes in illustration the internal maxillary artery as being the true "masticatory artery" in that it supplies the muscles of the lower jaw, the temporo-mandibular articulation, the pterygoid and temporal portions of the skull, and the third division of the trigeminal nerve. In recent years Shellshear [57] has applied Hilton's conception to the arteries of the brain, and he has attempted to associate the terminations of a particular vessel, not only with definite cyto-architectonic regions of the cortex as delimited by Campbell, Elliot Smith, Brodmann and others, but also with particular functional activities. The posterior cerebral artery is in this way, according to Shellshear, coupled with the mechanism of central vision, while the retinal artery is concerned with peripheral vision. It is interesting to examine the anterior cerebral artery in the light of these views.

The anterior cerebral artery, viewed phylogenetically, is intimately bound up with the development and regression of three separate structures, namely the rhinencephalon, the corpus callosum, and that portion of the motor cortex subserving leg movements.

In animals, from fishes upwards, the olfactory bulb is supplied by two vessels, known as the medial and lateral arteries of the olfactory bulb. There is in addition, commencing in the reptiles but more definitely in birds, a large ramus ethmoidalis which follows the olfactory nerve through an ethmoidal foramen. Within the nasal cavity it joins the ethmoidal branch of the internal maxillary artery to form an important plexus—the rete ethmoidalis—which supplies the mucous membrane of the nostrils and nasal cavities. These vessels are all large in calibre, though they vary in relative importance according to the species. In most mammals they outweigh the anterior cerebral arteries in magnitude, but they wane in importance with the decline in the rhinencephalon. They all arise primarily from the ramus cranialis of the cerebral carotid artery, but there are marked individual differences in the more immediate mode of origin. Thus, in fishes, the lateral and medial arteries of the olfactory bulb both arise from the carotid. In some of the reptiles and amphibians they take origin from the azygos anterior cerebral artery. The chief stem of the carotid artery in birds is continued forwards as the large ramus ethmoidalis; the anterior cerebral arteries are relatively insignificant. In mammals the ramus ethmoidalis is often called the anterior meningeal artery; it emerges at times from the anterior cerebral, but at times from the stouter marginal artery. The lateral and medial arteries of the olfactory bulb originate usually in the anterior cerebral, but also at times in the middle cerebral artery.

In man, as in the higher apes, the rhinencephalon and its vascular supply are relatively much less important. The branches of the anterior cerebral artery, particularly the prefrontal branch and at times Heubner's artery, continue to supply the olfactory bulb and peduncle and the tuberculum olfactorium. The most anterior portions of the olfactory pathways, as represented by the anterior pillars of the fornix, are also supplied by the anterior cerebral artery, but it is noteworthy that the posterior regions of the olfactory apparatus lie in the territories of other vessels. Obviously, the conception of the anterior cerebral artery as the artery of the smell-brain must be qualified: it is perhaps justifiable to regard it as the chief artery of the anterior rhinencephalon.

Prior to the development of the corpus callosum the backward prolongations of the anterior cerebral artery are insignificant. With the specialization, however, of the dorsal commissure in monotremes and marsupials, the retro-olfactory portion of the anterior cerebral artery enlarges and is carried backward. This process advances with the phylogenetic ascent, so that as its rhinencephalic supply wanes the importance of the anterior cerebral artery as an artery of the corpus callosum increases.

The function of the anterior cerebral artery in supplying the motor cortex is always, so far as one can judge, subserved by a separate collateral branch from the main trunk. In the cat, as in most lower mammals, this vessel is an extremely fine one and may itself arise from another branch of the anterior cerebral artery. In the stag, cow and horse, however, where there is a large marginal artery, the uppermost portion of the motor cortex is supplied by one of the terminal branches of this vessel. The simian and human paracentral lobules are supplied by a branch which usually arises from the main anterior cerebral artery trunk, though at times it arises in common with the posterior internal frontal.

No satisfactory explanation has yet been forthcoming of the dual arterial supply of the motor cortex in man and apes. This mode of supply appears to challenge the views of Hilton and Shellshear. If it could be shown, however, that throughout the mammalian series the anterior cerebral artery has supplied the cortical centres supplying the limbs used for progression, and that with the development of the prehensile fore-limb the anterior cerebral artery has continued to supply the leg area only, then there would be grounds perhaps for regarding this vessel as the "artery of progression." Until such evidence is forthcoming the assignment of a physiological significance to the anterior cerebral artery will remain open.

Although there is an approximate correspondence between the territories of the cerebral vasculature and the topography of various cytoarchitectonic zones, the idea of the functional significance of the individual arteries must not be strained. Such schematization would presuppose a simplification of the anatomical basis of cerebral function which is out of accord with our conceptions of neurophysiology.

SYNDROMES OF THE ANTERIOR CEREBRAL ARTERY.

On theoretical grounds it seems possible to distinguish between occlusions of the main trunk at various points, and thromboses of the individual branches of the anterior cerebral artery.

A.—*Occlusions of the Main Trunk.*

Here the most important differentiation has to be made between cases of thrombosis of the entire anterior cerebral artery and occlusion of the trunk after the emergence of Heubner's artery. Numerous other syndromes are theoretically possible, depending upon the site of occlusion with respect to the emergence of the various individual branches.

(1) *Total occlusion of the anterior cerebral artery (including Heubner's artery.)*

A thrombus in this position will cut off the blood supply from the whole area of distribution, namely, the mesial portions of frontal and parietal lobes and the subjacent white matter, the corresponding half of the corpus callosum, the head of the caudate and of the putamen, and the foremost half of the anterior limb of the internal capsule.

It is important to bear in mind that the thrombus must be of sufficient size to cover the point of emergence of the anterior communicating artery. If the thrombus is too short to reach this branch, the opposite anterior cerebral artery may distend the anterior communicating artery and take over the supply of both hemispheres. The result in such a case will then be almost identical with that of thrombosis of the recurrent artery of Heubner.

The chief clinical results may be stated as :—

Hemiplegia of severe degree ; some sensory loss over the paralysed lower extremity ; left-sided apraxia (if the hemiplegia is right-sided) ; mental change ; some degree of aphasia (if the lesion is left-sided).

The hemiplegia is due partly to the affection of the anterior part of the internal capsule and partly to disease of the paracentral lobule. The former will cause a severe degree of paralysis in the face, tongue and upper extremity (particularly in the proximal portion), while the latter affection will account for a marked weakness in the distal region of the lower extremity. There may be deviation of the head and eyes away from the paralysed side. The hemiplegia will usually be of the typical spastic variety and signs of pyramidal affection will be demonstrable in the increase in tendon-jerks and the presence of a Babinski response.

Softening in the cortex and subcortical white matter of the mesial portion of the post-central convolution will occasion some sensory impairment in the paralysed lower limb, particularly in its most peripheral part.

Destruction of the lateral half of the corpus callosum will interrupt the commissural fibres between the two frontal lobes and in this way is liable to produce an ideomotor type of apraxia in the left side of the body, provided that the motor power is intact. Should the right anterior cerebral artery be affected, the left-sided apraxia will be masked by the severe motor paralysis of the upper and lower extremities; the right arm and leg will be non-paralysed and eupraxic. Owing to the escape of the splenium which is supplied by the posterior cerebral artery, a visual type of apraxia is not observed.

Some degree of intellectual loss will be present, comprising retardation, confusion and disorientation amounting at times to an actual dementia. Loss of memory may be profound, and incontinence of urine and fæces may occur. Affective changes, including emotivity, euphoria and "Witzelsucht," have not been recorded. In severer cases, all degrees of clouding of consciousness may occur, up to complete coma.

Implication of the white matter in the centrum ovale may give rise to some degree of aphasia of the executive type, often accompanied by defects in articulation. Such changes are frequently temporary.

In the following case an occlusion of the first part of the anterior cerebral artery was revealed at autopsy.

Case 1.—B.M., female, aged 95, an inmate of Tooting Bec Mental Hospital since 1925. She was admitted as a case of senile dementia of mild degree. There were no obvious abnormal physical signs in the nervous system. In the course of the next five years the mental and physical states slowly deteriorated, and she was subject to occasional attacks. During the last year of her life she showed traits of puerilism, and would nurse a rag-doll which she had snatched from another patient and thereafter refused to surrender. On March 15, 1930, she fell whilst dressing; immediately afterwards she lost consciousness and became convulsed. A condition of right-sided hemiplegia was noted, with an extensor plantar response on that side. Coma deepened and she died three days later.

At the post-mortem examination, a rupture of the heart was discovered in the region of the conus arteriosus. In the brain, a recent softening was found in the orbital and mesial aspects of the left frontal lobe; this also extended posteriorly as far as the summit of the post-central gyrus. The genu of the corpus callosum was also involved. Trans-section through the left hemisphere revealed that the softening involved the cortex and subjacent white matter of the mesial portion of the frontal and parietal lobes. The head of the caudate was entirely destroyed, and the whole of the lenticular nucleus and the anterior limb of the internal capsule were softened. On dissection of the cerebral arteries a firm thrombus was found in the left internal carotid artery, completely filling the lumen and extending along the first part of the anterior cerebral artery. The middle cerebral trunk was not occluded. There was widespread sclerosis of the cerebral vessels.

It is unfortunate that in this patient the mental state and abruptness of the stroke rendered complete neurological examination difficult. From the pathological appearance it is obvious that there had been an occlusion of the main trunk of the anterior cerebral artery at its origin; the area of softening was greater, however, than the limits of supply of that vessel, suggesting that the perforating branches of the Sylvian, or even the anterior choroidal artery, may have been simultaneously involved.

Case X in Baldy's series [4] probably exemplifies a thrombosis of the anterior cerebral artery at the point of origin:—

F., aged 67, was admitted to hospital in a state of coma which had supervened three days previously. There was a complete right hemiplegia with brachial predominance. Head and eyes were deviated to the left. Ankle clonus and a Babinski response were obtainable on the right side. Stimulation of the inner aspect of the right arm produced an abduction movement with extension of the elbow. Involuntary movements were present in the fingers of the left hand. The patient's condition was too severe to permit an investigation of sensation or of tests for aphasia and apraxia. Death occurred on the eighth day. Post-mortem examination revealed, in addition to numerous small focal lesions, a softening in the anterior and inferior regions of the anterior cerebral territory, the anterior two-thirds of the caudate and lenticular nuclei and the anterior part of the internal capsule.

(2) *Occlusion of the anterior cerebral artery trunk after the emergence of the recurrent artery of Heubner and the anterior communicating artery.*

The syndrome resulting from a thrombosis of the artery at this site is one of great interest. It comprises:—

Hemiplegia with crural predominance. Indefinite sensory impairment. Left-sided apraxia. Mental change. Some degree of aphasia if lesion is in the left hemisphere. Psychomotor phenomena in the hemiplegic upper extremity.

In this case the hemiplegia is due to the direct affection of the leg area in the paracentral lobule, with implication of the adjacent motor area. Since the only parts of the motor cortex directly within the anterior cerebral territory are the uppermost and mesial portions, which are associated with movements of the lower extremity, the paralysis will be most intense in the region of the foot and ankle, and least in the face and tongue. Although signs of pyramidal involvement are usually demonstrable, the hemiplegia is often of the flaccid variety.

Sensory changes may be found in the affected half of the body, particularly in the lower limb, as a result of softening of the post-central gyrus.

Apraxia of the ideomotor type will be present in the left side of the body, whichever hemisphere is affected. Thus, in lesions of this type in the left anterior cerebral artery there will be a contralateral hemiparesis with a homolateral apraxia; right-sided occlusions will give ipsolateral hemiparesis with apraxia. Mental change occurs as in total occlusion of the anterior cerebral artery.

Speech defects of various types may occur with left-sided lesions. They comprise partly defects of an aphasic order, and partly those of a dysarthria; as a rule they are transient. In Baldy's case, echolalia and palilalia were also present.

Psychomotor defects in the paretic upper extremity comprise the phenomenon of forced grasping and groping (and possibly also of tonic innervation). The presence of these phenomena with the associated manifestations of "after-grasping" and "groping" can probably be associated, following Adie and Critchley's experience [1] of tumour cases, with disease of the posterior extremity of the superior frontal convolution.

Schuster, both singly and in collaboration with Pinéas, has directed attention to a phenomenon which occurred in association with forced grasping in some of his patients. On gentle stimulation of the skin in the neighbourhood of the lower lip, there resulted a pouting movement of the lips and at times a deviation of the point of the tongue towards the side of the contact (=*Ansaugen*).

The following abstracts illustrate the symptomatology of this type of arterial occlusion.

1907. *Liepmann and Maas* [41].—M., aged 70, developed a paralysis of the right leg in the course of twenty-four hours; later the right arm and right half of the face became affected and there was some defect of speech lasting a week. Mental confusion was at first present. The condition three and a half months later was as follows: Right hemiplegia, not affecting the tongue, speech a little slurred. Left apraxia and left agraphia.

1926. *Schuster and Pinéas* [56] (*Case Zeidler*).—F., aged 78, suddenly developed a left-sided weakness. Examination revealed a left hemiparesis with paralysis of the leg, no sensory loss, no aphasia, severe motor apraxia, left-sided grasping reflex and "after-grasping." "Ansaugen" was also present.

1926. *Schuster and Pinéas* (*Case Füllgraf*).—F., aged 60, right hemiparesis with maximum weakness in the leg. Tendon-jerks increased on the right side; right Babinski response. No sensory loss. Left-sided apraxia. Grasping phenomenon present in right hand.

1926. *Barré, Morin and Reys* [8].—M., aged 32; ten days after onset of a sudden headache patient had a fit. Four others followed within the next thirty-six hours. After the last attack he developed a right-sided flaccid hemiplegia with a Babinski response and died the following day.

1927. *Baldy* (*Case* 7).—F., aged 73, was examined in a state of semi-coma and found to have a right-sided flaccid hemiplegia with crural predominance. Babinski's sign was present on the right side. Sensation was apparently defective over the paralysed limb. No aphasia, but echolalia and palilalia were present. Left-sided apraxia. Memory defective but no gross intellectual enfeeblement.

1928. *Lhermitte, Schiff and Courtois* [40].—M., aged 71, developed transient weakness right arm and leg. Eleven months later he became temporarily confused and apraxic and the right leg became weaker. On examination two months later, there was found a right flaccid hemiplegia affecting chiefly the leg; ankle clonus on right, but no definite Babinski response. There was some executive and receptive aphasia. Tonic spasms appeared in the right arm resisting passive manipulations and the grasping phenomenon was present.

(3) *Occlusion of the main trunk after the emergence of the frontopolaris and prefrontal branches.*

The syndrome following this particular lesion is illustrated by the following personal case and also by the cases recorded by Bonhoeffer, by Foix and Hillemand and by Baldy.

Case 2.[1]—E. H., female, aged 22, was admitted to the National Hospital, Queen Square, on August 12, 1895, under the care of Dr. Bastian. There was a history of a fright in November, 1894, which was followed the next day by an "hysterical fit." Two weeks later she was noticeably vacant and absent-minded and early in the morning she was found by her husband in a state of semi-coma. There had been urinary incontinence. She could not understand what was said to her. During the day she had another "hysterical fit." She was found to be helpless down the right side and aphasic, but in the course of the following month the speech returned and she regained the power in her arm. The right leg remained for a time helpless, insensitive and œdematous and then began to recover. The previous history was unimpaired except for a "fright" in 1893, following which she lost her speech for a couple of weeks and was unconscious for three hours. There had been no paralysis. On examination she was found to be deaf and aphasic. She could only just hear a loud report in each ear; comprehension of written words was perfect. Her speech was described as "gibberish." There was slight weakness of the right lower face, but the tongue was not deviated on protrusion. Motor power seemed good, but there was a distinct diminution of sensation in the right leg. The tendon-jerks were diminished in that limb.

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[1] Also recorded by Mott [48] [49], with full pathological and clinical details.

After leaving the National Hospital in September, 1895, she improved till a month later when she had another fit; she was then sent to Barning Heath Asylum where she remained until February, 1896. At the time of her discharge her physical state was unchanged and she was cheerful and happy in demeanour. A year later, however, she became depressed and irritable; she frequently laughed and cried without reason; she was violent at times and had attempted suicide on one occasion. She was admitted to Claybury Asylum in March, 1897. There she was described as very emotional, irritable and depressed. She was totally deaf, but could understand written statements of a simple nature. Spontaneous speech was very sparse and badly articulated; she was dysgraphic. Physical examination revealed wasting and spasticity of the right leg without sensory impairment; bilateral ankle clonus with Babinski responses; coarse tremor of left arm.

She was transferred to Colney Hatch Asylum in June 1898; while in that institution she showed weakness of the right half of the face and tongue; both legs were spastic, especially the right. Tremor was present in right arm. Sensibility was intact but possibly delayed. She remained completely deaf. In June, 1902, she died.

Autopsy revealed, in addition to a definite mitral stenosis, three foci of softening in the brain:—

(1) In posterior third of T.1 (left) and of T.2 posteriorly, and almost all the supramarginal gyrus.

(2) A smaller area in the right hemisphere involving the posterior part of T.2, and the postero-inferior part of the supramarginal convolution.

(3) A softening in the middle portion of the mesial surface of the left hemisphere, involving most of the paracentral lobule and gyrus cingulus. The territory probably corresponded with the distribution of the anterior cerebral artery posterior to the *frontopolaris* branch.

It is difficult, of course, accurately to correlate the clinical with the pathological data, owing to the multiplicity of the foci, as well as to the indefiniteness of the clinical history. The first stroke probably corresponded with an embolus causing an infarct on the left temporal lobe; and the second attack with the lesion in the opposite hemisphere. As a result, the patient became totally deaf and aphasic. The third fit probably corresponded with the occlusion of the left anterior cerebral artery.

One is probably justified in associating the spasticity and weakness of the right leg, accompanied at one stage by œdema and by sensory impairment, with the infarcted area in the territory of the anterior cerebral artery. The mental changes are possibly connected with the damage to the left frontal lobe, though more probably the result of the multiplicity of cortical and subcortical areas of destruction.

The following case, recorded by Bonhoeffer [18] in 1914, may also be quoted in this connection :—

M., aged 51, in September, 1909, had a sudden fall without loss of consciousness; this was followed by difficulty in speaking. The next day he fell again, this time unconscious; on recovery was speechless. A second stroke occurred on the day following. Examination revealed a right spastic hemiplegia with no voluntary movements in leg. The tendon-jerks were brisker on the right side but there was no Babinski response. The arm gradually improved but showed later a definite catatonic tendency (*Katalepsie*), together with forced grasping. There was a bilateral apraxia, and a mixed type of aphasia.

Autopsy revealed four foci of softening:—

(1) A recent hæmorrhage in the territory of the right lenticular artery.

(2) A small softening in the left parieto-occipital lobe.

(3) A small focus in the anterior part of the internal capsule due to occlusion of the lenticulo-striate artery.

(4) An old softening in the territory of the left anterior cerebral artery with destruction of the corpus callosum as far back as the splenium, and of the anterior four-fifths of the superior frontal gyrus, and the anterior two-fifths of the median frontal convolution.

Foix and Hillemand (*Case Vig.*) (= *also Case VI. of Baldy.*)—M., aged 62, developed four years before, a weakness of her left side of sudden onset. On examination there was found a left hemiplegia affecting the foot severely; the tendon-jerks were brisker on that side and there was a clonus and a Babinski response. Sensory changes in affected limbs. Marked intellectual enfeeblement; no aphasia. Left ideomotor apraxia.

In Case IV of Foix and Hillemand's paper there was an occlusion of the main trunk in this situation, but the clinical examination was unfortunately incomplete. The only details available are that the patient had a left hemiplegia with contracture, affecting particularly the leg, and a left homonymous hemianopia. Forced laughter and crying were also present. The patient was admitted to hospital in a state of coma with deviation of the head to the right and with a flaccid right-sided hemiplegia.

In addition to the infarction in the territory of the right anterior cerebral artery there was a terminal softening from occlusion of the posterior cerebral artery. The left hemisphere contained a small focus in the prefrontal lobe.

(4) *Occlusion of the main trunk between the origins of the middle internal frontal and the posterior internal frontal branches.*

In the following case, recorded by Claude and Loyez [19], the area of softening corresponds with a thrombosis of the anterior cerebral artery in this situation :—

Male, aged 51, sustained as the result of a stroke a right-sided hemiplegia with defects of speech and vision. His symptoms improved, with the exception of the weakness of the right upper extremity. Five months later a second stroke was followed by a sensation of burning in the left upper limb, and there were vasomotor changes and cyanosis. Examination showed a condition of right-sided hemiparesis with brachial predominance ; tendon-jerks were brisker on the right side ; both plantar responses were flexor in type. There was no gross defect of sensation, but there were errors of topognosis and of tactile discrimination equally pronounced over both halves of the body. There was a left-sided apraxia of mixed ideatory and ideomotor type. Psychical changes included defect of memory, inability to perform mental calculations and inability to read or write. There was no aphasia, but the speech was somewhat stammering.

Three years later a fresh stroke occurred and was followed by the appearance of pseudo-bulbar signs. Death occurred two years afterwards.

(5) *Occlusion of the main trunk between the origin of the posterior internal frontal and paracentral arteries.*

This particular type of lesion is probably exemplified in the case recorded by Goldstein [29], [30] :—

A female, aged 57, developed a left-sided hemiplegia which improved, but left a severe permanent weakness in the leg. Synchronously with the return of strength certain disorders of mobility made their appearance. Thus, in addition to a unilateral apraxia with marked poverty of spontaneous movement, the phenomenon of tonic innervation was present. Amorphous movements of a " pseudo-spontaneous character " made their appearance when she voluntarily attempted an action. She was unable to write with the left hand.

B.—*Occlusion of Individual Branches of the Anterior Cerebral Artery.*

Unfortunately our knowledge as to the clinical effects of thrombosis of the various branches of the anterior cerebral artery is still very incomplete, but a few records are quoted to illustrate one or two such instances.

(1) *Occlusion of Heubner's artery.*

This was present in one personal case in which there were actually two thromboses in the anterior cerebral branches. There was an exact correspondence in the size and position of one infarcted area with the territory of this vessel, and the shrunken and occluded artery of Heubner was easily demonstrable.

Case 3.—C. W., male, aged 57, was admitted to the National Hospital, Queen Square, under the care of Dr. F. M. R. Walshe on November 8, 1928. Five months previously he had experienced a sudden loss of speech, accompanied by a slight weakness of the right arm. This became worse two days later. Three weeks afterwards, a weakness was noticed in the right leg. For the three months immediately prior to admission his speech as well as the paresis of the leg had been improving, but the arm remained completely helpless. Some psychical change, such as irritability and forgetfulness, had been noticeable.

He was a stout florid man with complete inability to speak; he could understand and execute simple commands, however, but could not read. There was no apraxia. He showed some emotional incontinence.

There was possibly a right-sided homonymous hemianopia. The right pupil was larger than the left. Slight weakness was present in the right half of the face, palate and tongue.

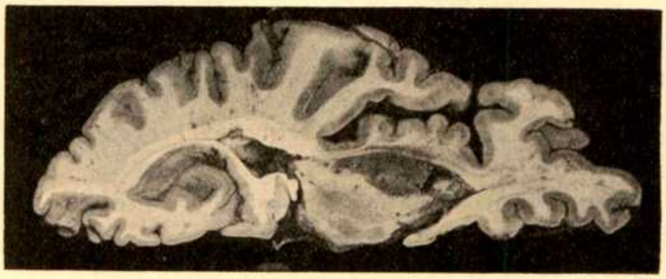

FIG. 12.—The region of the basal ganglia of the left hemisphere from *Case* 3. There is a softening in the head of the putamen and caudate nucleus, exactly corresponding with the distribution of Heubner's artery.

The right arm was spastic and no voluntary movements were possible with the exception of a few feeble movements in the fingers. When the arm was held away from the trunk a rhythmical tremor was evident. There was some slight weakness of the right leg with increase of tonus. Sensation was apparently intact. The abdominal responses were absent and both plantars were of the extensor variety. Tendon-jerks were brisker on the right.

Blood-pressure measured 210/110; the radial and retinal arteries were distinctly sclerotic. The heart sounds were tic-tac in character and the second aortic sound was ringing. Blood Wassermann reaction was negative.

The patient died on December 2, 1928. Autopsy revealed three foci of cerebral softening:—

(1) A large focus in the left hemisphere in the territory of the middle and posterior internal frontal branches of the anterior cerebral artery.

(2) An old small softening immediately beneath the cortex of the left angular gyrus, involving the optic radiations.

(3) A softening in the head of the putamen and caudate nucleus on the left side. The anterior half of the fore-limb of the internal capsule was also involved. (See fig. 12.)

In this case it is likely that the third-mentioned lesion, due to the occlusion of Heubner's artery, corresponded with the first stroke, while the weakness of the right leg, appearing three weeks later, is to be associated with the thrombosis of the middle and posterior internal frontal branches. If this is so, then the severe degree of weakness of the right upper extremity—involving the whole limb with conservation of feeble mobility in the fingers—the spasticity and the tremor are referable to this lesion. The slighter degree of paralysis of face, palate and tongue are also connected in all probability with this particular focus. It is probable that the aphasia is in part referable to the lesion of Heubner's artery, though alexia is clearly due to the affection of the angular gyrus.

(2) *Occlusion of the frontopolaris branch.*

There is no clinical record of a softening confined to the territory of the frontopolaris branch, though Foix and Hillemand have given an illustration in their paper of the brain of such a case.

(3) *Occlusion of the middle and posterior internal frontal branches of the anterior cerebral artery.*

The symptoms of this type of thrombosis are exemplified by the ollowing three cases:—

Case 4.—F., aged 33, was admitted under the care of Dr. J. Odery Symes to the Bristol General Hospital on August 5, 1924, in a state of coma. The history was that she had been confined twelve days previously: no abnormality had been noted until 2 a.m. of the twelfth day, when she said she could not move her body although she was actually able to move her limbs and appeared perfectly sensible. At 7 a.m. she began shaking violently and half an hour later she lost consciousness. When admitted at 2 p.m. she was still unconscious; respirations were stertorous. She became "rigid and shaky" when handled. Pulse rate 152. Respiratory rate 38. Temperature 101° F. Blood-pressure 130. Urine normal.

During the course of examination she went into a generalized fit. There was no pupillary abnormality; the knee-jerks were present on both sides, although they disappeared later the same day. A bilateral Babinski response was obtained. Several other fits supervened during which the right half of the body was rigid and immobile, while the left arm and, to a lesser extent the left leg, twitched. Fits followed in rapid succession, and the unconsciousness became more profound. The march of the attack became more definite, commencing in the eyelids and face and proceeding thence to the left arm and finishing in the hand; no other limb became convulsed. Head and eyes were deviated to the left. The cerebrospinal fluid was not under obvious tension. It was yellowish in tint and slightly turbid; on standing a spider-web clot formed. Total protein 0·3 per cent: globulin in excess; cell count 350 per cmm., of which 85 per cent. were polynuclears. Culture sterile. The temperature rose to 107° F. the next day, the respirations became more laboured and death occurred forty-eight hours after the onset of cerebral symptoms.

Autopsy revealed an infarct in the region of the middle and posterior branches of the left anterior cerebral artery.

Case 5.—J. W., male, aged 42, was admitted to the National Hospital, Queen Square, on May 26, 1924, under the care of Dr. J. L. Birley, suffering from Jacksonian attacks and weakness in the left leg. The history dated from 1916: Whilst a soldier on parade he was observed to stagger and was sent to the guard room as drunk. Whilst under arrest he had a fit which was followed by paralysis of the left side of the body and some affection of speech. In the course of a few weeks the speech defect cleared up and strength returned to the arm. Later the leg regained power. The following year another fit occurred but left no sequelæ. Thereafter other attacks followed in great number. There were two chief types of fit: (*a*) attacks consisting in a "funny feeling in the head," together with twitching of the left arm and knee, without loss of consciousness, and (*b*) major fits with unconsciousness.

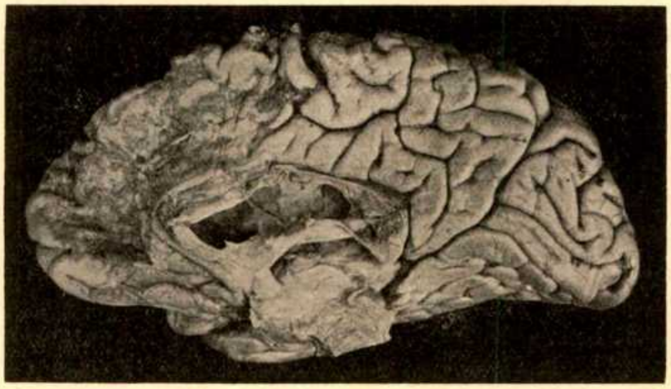

FIG. 13.—Large focus of softening in the right hemisphere from *Case* 5, corresponding with the distribution of the middle and posterior internal frontal branches of the anterior cerebral artery.

Previous health was uneventful except for syphilis contracted at age of 18.

His physical condition on admission was as follows:—

Optic discs somewhat blurred; nystagmus on lateral ocular deviation; clumsiness and dysdiadochokinesis of the left upper extremity. The left leg was spastic and weak. There was an indefinite blunting to pin prick over the left hand. The tendon-jerks were brisker on the left and there was a left Babinski response. The diagnosis was made of a right-sided tumour in the motor area, but an exploratory operation failed to reveal any definite abnormality.

For a year following the decompression he was free from fits. They then returned and his left leg became weaker so as to interfere with his walking.

He was re-admitted to the hospital on September 23, 1929, under the care of Dr. J. P. Martin. He now showed definite psychical changes, especially gross retardation. His expression was vacant.

The disc edges were still hazy. The pupils were now Argyll-Robertson in type. Both hands were tremulous and somewhat ataxic; there was dysdiadochokinesis in the left arm, and the right grasp was definitely stronger. The left leg was weak and spastic and lay in an attitude of extension. The reflexes were brisker on the left side, and both plantar responses were flexor in type. No sensory change was demonstrable.

The diagnosis was made of dementia paralytica and the patient died on October 28, 1929. Autopsy revealed the macroscopic changes of general paralysis of the insane which were substantiated by histological examination. In addition there was an old softening in the territory of the anterior cerebral artery and the middle internal frontal was reduced to a fine impervious thread. The posterior internal frontal, which arose as a branch of the middle internal frontal artery, was similarly affected. The main trunk of the anterior cerebral artery was not occluded. (See fig. 13).

In Case 3 it will be remembered that three softenings were demonstrated at an autopsy; one lay in the angular gyrus, and one in the basal ganglia in the territory of the artery of Heubner. The third focus occurred in the area supplied by the middle and posterior internal frontal arteries (see fig. 14). The sudden attack of weakness in the right leg occurring three weeks after the original attack can probably be referred to this particular lesion. We may, therefore, refer to this as the third example of occlusion of the middle and posterior internal frontal vessels.

Of these three cases the first is obscured by the severity of the general symptoms which excluded an intimate examination. The two most important focal manifestations were left-sided convulsions and deviation of the head and eyes towards the left. In the light of the pathological evidence this can be correlated with the left-sided cerebral infarction which, from the suddenness of its onset, must have caused a severe degree of right-sided hemiplegia and deviation of head and eyes to the opposite side. The non-affected right half of the body, therefore, showed the only involuntary movements in what were otherwise generalized epileptiform convulsions.

In the second case the most obvious findings consisted in a spastic crural monoplegia with an extensor plantar response, together with some degree of awkwardness of the ipsolateral upper limb. The occurrence of local seizures commencing in the left hand were here probably in the nature of irritative Jacksonian fits, and were frequently unaccompanied by loss of consciousness.

The third example (i.e., Case 3) is complicated by the plurality of lesions, but one is probably justified in referring the spasticity and weakness of the right leg to this particular focus.

(4) *Occlusion of the paracentral artery.*

Here the area of ischæmia involves the cortex and subjacent white matter of the paracentral lobule including that portion of the motor cortex associated with the innervation of the foot and lower leg. This lesion has been verified in the cases recorded by Long (1907) [42] [43], Wilson (1923) [65], and by Winkelman (1924) [67].

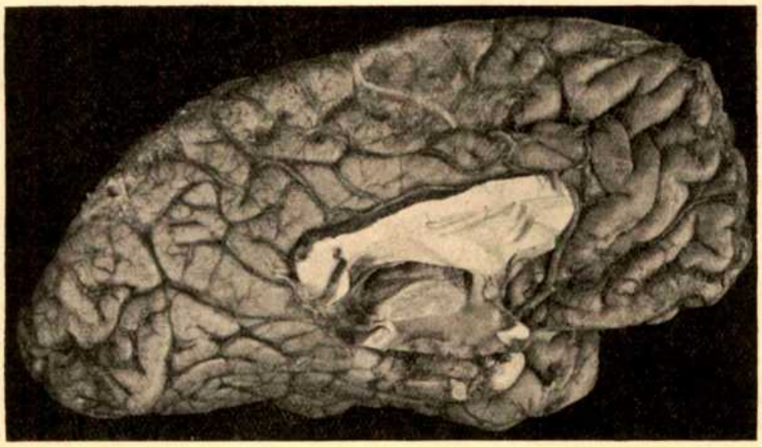

FIG. 14.—Brain from *Case* 3, showing a softening in the area of supply of the middle and posterior branches of the left anterior cerebral artery.

In Long's patient, a man of 72, there was a history of a sudden weakness in the left leg; the arm and the face were not affected. The movements in the leg were found to be limited in range and feeble in strength, the foot lay in an equinovarus attitude. The knee-jerk was exaggerated on that side, and although the plantar response was extensor in type, there was no ankle-clonus. Five years later the physical signs were unchanged. The site of the lesion was determined at autopsy.

Wilson's Case 1 was that of a woman aged 74, who three weeks previously had developed a sudden weakness of the right foot. In a few hours this spread to the leg and increased in intensity. On examination, the leg was œdematous and in a position of eversion. No voluntary movement was possible; passive manipulations evoked pain. There was slight clonus at the right ankle and the plantar response on that side was of the extensor variety. Sensation was normal. Autopsy revealed a softening of the paracentral lobule and uppermost tip of the motor cortex.

Winkelman's Case 2 concerned a coloured woman aged 38 who developed a sudden paralysis of the left leg with numbness and tingling. Six months later she died from a second stroke. At autopsy, an old softening was found in the paracentral lobule, in addition to a recent thrombosis in the internal capsule.

The outstanding clinical feature in the last group of cases has been a weakness of the contralateral lower limb. In some instances it exists alone in a crural monoplegia, while at other times it accompanies a lesser degree of weakness of the arm, face and tongue on the same side. The maximum weakness is found in the distal portion of the leg. In most instances the affected limb is spastic, with exaltation of the tendon-jerks, ankle-clonus, and an extensor plantar response. In not a few the limb was markedly œdematous; sensory changes are also present at times.

On looking over the clinical results of thrombosis of the anterior cerebral artery at various points and of occlusion of its various branches, certain symptoms stand out by reason of their frequency. Three symptoms in particular attract attention, namely, paralysis of the lower extremity, psychomotor disorders in the ipsolateral upper limb, and ideomotor apraxia affecting the left arm, whether that limb be ipsolateral or contralateral. The characteristics of the crural monoplegia have already been noted. This particular symptom is the most striking of the manifestations of disease of the anterior cerebral artery, and only in the case of thrombosis of the main trunk between the origin and the anterior communicating vessel is the monoplegia masked by the addition of a severe capsular type of hemiplegia. Since the paracentral lobule represents the only area in the territory of the anterior cerebral artery which possesses an obvious and localized clinical significance, the explanation of the frequency of crural monoplegia is obvious.

Cases of paralysis of one leg arising suddenly in the course of a cerebral arteriosclerosis or cases of hemiplegia with crural predominance are not very uncommon. In the course of the last three years seventeen such cases have come under my notice. It is rare, however, for pathological verification to be forthcoming in such cases as the causative lesion is rarely sufficiently severe as to cause death.

Lesions of the cerebral arteries, other than the anterior cerebral, are very unlikely to cause a marked paralysis of one lower extremity without affecting equally severely the arm, face or tongue on that side. The anterior cerebral artery, however, by reason of its exclusive supply of the leg area—which receives no blood from other sources—characteristically produces, when diseased, an affection of the lower extremity. It is highly probable that the great majority of cases of crural monoplegia of sudden onset, occurring in the course of a cerebral arteriosclerosis, are due to lesions of the anterior cerebral artery or its branches.

There is one particular vascular lesion, however, which closely resembles in its clinical features occlusion of the paracentral artery—namely, thrombosis of the vein of Rolando. In Waggoner's case [63] a man of 76 awoke one morning to find his right leg paralysed. The arm was also slightly weak but rapidly regained its strength. On examination, the right leg was found to be weak and the whole right side was incoordinate. Tendon-jerks were brisker on the right, the abdominal reflexes were absent on that side but there was no Babinski response. The only sensory loss consisted in an astereognosis of the right hand. At autopsy a large thrombosis of the left Rolandic vein was found overlying a plexiform hæmangeioma.

Closely analogous with the foregoing are the cases of injuries of the superior longitudinal sinus, resulting from shrapnel or gunshot wounds of the vertex of the skull, as described by Holmes and Sargent [36]. Whilst in the majority of cases symptoms of bilateral and symmetrical distribution were the result, sometimes one side of the body was affected alone; this was the result of an injury directed to one side of the middle line, blocking the circulation through a lateral lacuna or in the veins as they enter the sinus. Of their series of twenty patients, five showed symptoms affecting one leg only. The clinical results of such a lesion comprised a paresis of the lower extremity most marked in the distal segments; severe rigidity with exaggeration of the tendon-jerks and extensor plantar responses; a cortical type of sensory loss, as shown by gross defect of postural sensibility and tactile discrimination, with little or no impairment to light-touch, pain or temperature. The attitude of the paralysed limb was usually one of extension with adduction and internal rotation; the big-toe was often maintained in the so-called "Babinski attitude."

Ipsolateral psychomotor disorders are important in most cases of thrombosis of the anterior cerebral artery; they are absent from cases of thrombosis confined to the paracentral branch. Although probably of frequent occurrence, it is possible that at times they are overlooked, particularly when mental change or obfuscation of consciousness complicates the picture. Characteristically, they comprise the phenomena of forced grasping and groping. In Goldstein's case tonic innervation was present, probably in addition to a grasp reflex. Other psychomotor anomalies include the presence of catatonia and the "pouting" and "sucking" reflexes noted in Schuster's patients. Goldstein's patient also showed a distinct hypokinesia and an absence of "movement-intention." Voluntary movements were accompanied by the appearance of amorphous, pseudo-spontaneous movements, and there was a severe disturbance of optical imitation.

Softening of the corpus callosum occurs in many of the types of occlusion of the main arterial trunk, and gives rise to the appearance of apraxia in the left side. The apraxia is of the ideomotor variety, and is shown by the patient's inability to carry out a movement to command, such as saluting, waving the hand or blowing a kiss. The apraxia is always unilateral and left-sided, since, according to Liepmann's conception, the centre controlling eupraxia is situated in the left supra-marginal region and is associated with the motor centres of both sides. The connections between the left supra-marginal gyrus and the right motor cortex pass by way of the corpus callosum. Damage to this commissure will, therefore, result in left-sided apraxia.

When the thrombus lies in the right anterior cerebral trunk at the point of emergence of Heubner's artery, the resulting severe degree of hemiplegia will obscure the apraxia.

BILATERAL LESIONS.

The presence of multiple foci in a case of cerebral arteriosclerosis so obscures the symptomatology that localization of the individual lesions becomes almost impossible. This is particularly true when the softenings lie in the territories of different cerebral arteries, such as the posterior cerebral artery on the one side and the Sylvian of the other. In the case of the anterior cerebral artery, however, it would seem theoretically possible to diagnose a bilateral symmetrical lesion, on account of the peculiar distribution of motor weakness. Thus a sudden weakness of one leg, followed later by a sudden weakness of the other, together with spasticity and signs of pyramidal defect, and little or no sensory change, would be suggestive of a bilateral affection of the anterior cerebral arteries. It is possible that some of the cases of so-called "senile paraplegia" belong to this group.

Case 6 illustrates the occurrence of bilateral, symmetrical softenings situated within the territory of branches of the anterior cerebral artery.

M. J., female, aged 88, an inmate of Tooting Bec Mental Hospital since 1913. She was admitted as a case of secondary dementia, and there was no gross abnormality found in the nervous system. Marked arteriosclerosis was present. During the seventeen years she was under observation she gradually deteriorated; there was at no time any definite illness except for occasional appearance of œdema and albuminuria. There was never any evidence of a stroke. She steadily became weaker and died in January, 1930, of heart failure following bronchitis.

At the autopsy there was found an old infarction of the left ventricle of the heart. The cerebral blood-vessels were grossly degenerated. There was a bilateral softening lying in the orbital aspect of both frontal lobes. The area was a little larger in the left hemisphere where it involved the pole of the frontal lobe as well as the gyrus rectus. On the right side the gyrus rectus alone was destroyed. An old porencephaly was present at the apex of the left temporal pole.

The softenings evidently lay within the territory of the prefrontal branch on the right side, and of the prefrontal and frontopolaris vessels on the left.

In the following case, a bilateral lesion in the territory of the anterior cerebral arteries produced a spastic paraplegia of cerebral type. The syndrome resulted, however, from a single lesion on account of a congenital peculiarity in the arterial distribution whereby the left anterior cerebral artery supplied both hemispheres:—

Case 7.—S. P., male, aged 45, was admitted to the National Hospital, Queen Square, under the care of Dr. J. L. Collier on November 26, 1920. Eleven months previously, on being informed that he had lost all his savings, his legs became immediately stiff and tremulous, and there was great difficulty in walking. His symptoms improved somewhat after three weeks, but became worse again five weeks before admission. There was some slight difficulty in micturition but no other sphincter disorder. Since the onset of his symptoms he had become impotent. There had been some psychical change within the past year; his memory was not so good, he was slower in his actions and his employers noticed that his work had fallen off so that he could no longer use a micrometer.

On examination, the right pupil was found to be larger than the left, but both reacted normally; there was a slight bilateral ptosis, and a few ill-sustained nystagmoid jerkings on lateral deviation of the eyes. The other cranial nerves were normal. There was no loss of motor power in the arms, but the tonus was somewhat increased and there was a distinct catatonic tendency. Both lower limbs were very spastic and the right leg was extremely weak, especially in the distal segments. There was no sensory loss other than a defect of postural sensibility in his toes on the right foot. The tendon-jerks were exaggerated on both sides and there was a left-sided ankle-clonus. The abdominal and cremasteric responses were present and both plantar reflexes were extensor in type. The cerebrospinal fluid was normal. Blood-pressure was 240.

Progress notes: On December 6, 1920, he suddenly cried out with intense headache, vomited and then lost consciousness. Coma deepened the next day and respirations became Cheyne-Stokes in type. A definite spasticity was now noticeable in the arms; a second lumbar puncture revealed a blood-stained fluid. He died on December 12, 1920.

Autopsy revealed a marked degree of sclerosis of the cerebral blood-vessels. There was a quantity of blood free in the subdural space. More careful examination of the cerebral arteries showed that the right anterior cerebral artery was extremely small in calibre and supplied only the most anterior portion of the frontal pole. At the level of the genu the left anterior cerebral artery, which was of greater size than the right, bifurcated and sent one branch across the middle line so as to supply the mesial aspect of the right hemisphere. In this way the left anterior cerebral artery was supplying the cortex, including the paracentral lobules, of both halves of the brain. A thrombosis of the first part of the main trunk of the left anterior cerebral artery was present, causing an ischæmia of the cortical areas corresponding with both lower limbs.

A small aneurysm was present on the right middle cerebral artery, as it lay in the Sylvian fissure.

Weigert-Pal preparations of the medulla and spinal cord showed a bilateral degeneration of the pyramidal tracts equal in degree on the two sides.

Cases of bilateral paralysis due to verified lesions of both anterior cerebral arteries are found in Baldy's fifteenth case and Schuster's [54, 55] case Warkow. The former was a woman who had a left hemiplegia with crural predominance, and left-sided hemianopia and forced laughter and crying. She was admitted to hospital on account of a sudden right-sided hemiplegia of flaccid type. Full examination was not possible as she was comatose. At autopsy three softenings were found; one in the territory of the right anterior cerebral artery, a cuneiform focus in the mesial portion of the left prefrontal lobe, and a recent softening in the territory of the right posterior cerebral artery.

Schuster's patient (Warkow) was an old man, aged 73, who had two strokes within four years. As a result he became paralysed in both legs and demented. He made no spontaneous utterance, and was disoriented in space and time. The right corner of the mouth was weak; the right hand moved restlessly in different attitudes. The left forearm was held tightly across the chest with the fist clenched. With the right hand the patient clutched the bedclothes firmly or else grasped neighbouring objects, such as the examiner's pencil, stethoscope, &c., and force had to be used to make him release the objects. Both legs were weak and there was an increase of tonus on the left side. The tendon-jerks were increased, especially on the left; the plantar responses were in extension. At post-mortem examination there was a bilateral softening of the anterior cerebral arteries.

The cases of bilateral symmetrical foci of softening in the prefrontal lobes recorded by Zacher [69], and by Mabilles and Pitres [44], may also be examples, but it is difficult to be certain from their pathological descriptions which particular vessels were occluded.

In addition to these instances of abrupt bilateral lesions of the anterior cerebral arteries, it is possible that there may also occur progressive affections of the two arterial trunks, so as to cause gradual bilateral manifestations of a paraplegic order. Thus in Marie and Foix's case [46] of cerebral paraplegia from progressive subependymal necrosis, a condition of paraplegia in flexion, dementia, dysarthria and emotional incontinence developed in a woman of 70. The pathological process consisted in an atrophy of the corpus callosum, and a progressive softening of the upper group of pyramidal fibres in their transition from the paracentral lobule through the white matter. Analogous cases have also been reported by van Bogaert and Ley (1926) [15].

Finally, one may mention briefly the condition of progressive degeneration and gliosis of the corpus callosum described by Marchiafava [45] in alcoholic subjects. Although this process is usually regarded as due to toxic action of the alcohol, Bonfiglio [17] has pointed out a local sclerosis of the neighbouring blood-vessels, and has suggested that the process is an ischæmic one, due to a progressive affection of the branches of the anterior cerebral artery.

ANEURYSM OF THE ANTERIOR CEREBRAL ARTERY AND ITS BRANCHES.

The anterior cerebral artery is one of the less common vessels to be the seat of aneurysm formation. Thus Peacock found aneurysms in the anterior cerebral or anterior communicating arteries in 9 out of 89 cases; in Krey's series of 142 cases an aneurysm occurred in the anterior cerebral artery in 11; Gowers found aneurysms on the anterior cerebral artery 14 times, and on the anterior communicating artery 8 times in his 154 cases. Van Hoffmann recorded 78 new cases of intracranial aneurysm, and placed the anterior communicating third and the anterior cerebral artery sixth or last in his list of common sites. Fearnsides [26] found in his 51 cases that the aneurysms arise from either the anterior cerebral artery or the anterior communicating artery in 15 cases.

In an attempt to analyse the cases of aneurysm of these vessels only those instances will be studied in which the site of the lesion was clearly defined at autopsy. The symptomatology then resolves itself into two main groups: first, the clinical evidences due to the size of the aneurysm and its contact with neighbouring structures; and secondly, the results of rupture or leakage.

In the great majority of cases there have been no focal or general signs of localizing value, and the demonstration of an aneurysm at autopsy has in many instances been unsuspected. Amongst the focal signs, affections of the first and second cranial nerves on one side are important. There results a unilateral anosmia and a progressive dimness of vision in one eye, advancing to complete blindness. The defect in the visual fields comprises a progressive scotoma which ultimately fuses with an incoming peripheral loss. Ophthalmoscopy reveals optic atrophy. Depression, and later abolition, of the pupillary reflex to direct light is found in the affected eye, although the consensual light response is maintained. In one case of Fearnside's the blind eye was totally anæsthetic.

When the aneurysm arises from the anterior communicating artery, pressure may be exerted upon the optic chiasma so as to produce ultimately a bitemporal hemianopic defect. This occurred in an interesting case of Weir Mitchell's [47] where the tumour grew from an anomalous vessel connecting the two internal carotid arteries, and which probably represented a doubling of the anterior communicating artery. The presence of other so-called "pituitary signs" usually indicates an aneurysm arising from the internal carotid.

Diplopia, without an obvious ocular palsy, may also result from direct pressure upon oculomotor nerves.

Erosion of the sella turcica or other portions of the floor of the skull may be demonstrable by X-rays, and there may also be revealed incomplete ring-like suprasellar shadows in cases of calcification of the aneurysmal sac.

Although in most cases no bruit is audible on auscultation of the skull, the patient may nevertheless complain of tinnitus. An insane patient of Beadle's, in whom an aneurysm of the anterior cerebral artery was afterwards demonstrated, complained for many years of a "waterfall inside the head."

It is noteworthy that in no confirmed case was there any clinical evidence of occlusion or other sign of interference with the functional activity of the anterior cerebral artery.

In addition to the signs of local pressure which are occasionally demonstrable, certain general manifestations may occur as with aneurysm elsewhere. Thus, paroxysms of headache are not uncommon, while drowsiness may also be observed. Papillœdema occasionally occurs and the combination of swelling of the optic disc in one eye, and atrophy in the other, is a particularly suggestive phenomenon. Mental changes may be present in a few recorded cases, but it is very doubtful to what extent these are directedly connected with the presence of the aneurysm.

The clinical manifestations of rupture or leakage of blood from the aneurysm are very similar wherever the site of origin of the lesion. It is rarely possible to predict from the clinical signs that the aneurysm lies on the anterior cerebral artery. In some cases there have arisen signs of a mild paretic order on the side of the body opposite to the blind eye. Ptosis has been observed in a few cases, sometimes bilateral, but at times in the opposite side only; paralyses of ocular movements may occur, but they are not of localizing importance. Dilatation and reflex immobility of the pupil on the side of the aneurysm may occur, but has also been described in the opposite eye. In all cases of rupture of aneurysms growing from the anterior portion of the circle of Willis, hæmorrhage may track along the optic nerve-sheaths, but this sign cannot be regarded as diagnostic of aneurysm of the anterior cerebral artery.

In our present state of knowledge, therefore, it is doubtful whether it is possible with any confidence either to lateralize or to localize an aneurysm of the circle of Willis. This holds true for the case of both the ruptured and unruptured aneurysm. Although it is frequently possible to predict whether the aneurysm lies in the anterior or the posterior portion of the circle of Willis, it is not possible to predict with certainty whether the internal carotid, the Sylvian, the anterior cerebral or the anterior communicating artery is the region affected.

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A THEORETICAL APPLICATION TO SOME NEUROLOGICAL PROBLEMS OF THE PROPERTIES OF EXCITATION WAVES WHICH MOVE IN CLOSED CIRCUITS.

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THE phenomena of spontaneous involuntary movements have never been satisfactorily explained. For many years neurologists have attempted to understand them solely in terms of Hughlings Jackson's conception of the release of a "lower" centre from the regulative or inhibitory control of a "higher" one. It cannot be claimed that these efforts have been very successful. Indeed, the absence of adequate pathological or experimental data to support this view is particularly striking when one recalls how fully the doctrine has been worked out by Sherrington and his school for the functional relationship of the brain-stem and cord to higher levels. This sharp contrast between the fruitful use of the conception in one direction, and its futile application in another, leads one to suspect that the phenomena involved may be fundamentally different.

There is, in fact, one quite obvious difference between spontaneous involuntary movements on the one hand, and, on the other, the experimentally investigated manifestations of inhibition and release. The former are purely pathological processes ; the latter are all components of normal function, e.g., postural tonus, fragments of normal movement patterns, and myotatic reflexes. In the experimental study of these mechanisms, something normal may be exaggerated (i.e., "released from inhibition") ; or, by appropriate stimuli, some normal response may be decreased (i.e., "inhibited") ; but no chaotic patterns of new movements are produced. If, therefore, one attempts to explain the presence or absence of spontaneous involuntary movements by processes of release and inhibition, it is their actual *creation* by release and their *total extermination* by inhibition which must be accounted for. This is not merely a normal mechanism undergoing increase or diminution ; it presupposes a process of inhibition and release which actually goes beyond experimental demonstration, and which leaves untouched the problem of what mechanism it is which is being released or inhibited.

Secondly, it must be emphasized that afferent stimuli produce postural tone and myotatic reflexes, not merely under the abnormal conditions of decerebration, but normally as well. On the other hand, it has not yet been proved that spontaneous involuntary movements depend in any way upon an influx of afferent stimuli. But even if it were shown that the elimination of all afferent impulses abolished such movements, it would be justifiable to conclude only that, without afferent impulses, no spontaneous movements can occur. It would remain obvious that since afferent stimuli are always occurring normally, and since spontaneous involuntary movements do not occur normally, therefore the afferent stimuli alone are not the essential mechanism although they may be a *sine qua non* of the phenomena.

In short, these are two different kinds of phenomena; one of them normal but subject to pathological exaggeration or diminution, the other found only in abnormal states; one of them directly produced by proprioceptive stimuli, the other dependent upon afferent impulses under abnormal conditions only, if at all. Obviously what may be an adequate explanation of the quantitative variations of the one can only play at most a contributory rôle in producing the other.

Out of the manifold possibilities with which the central nervous system is endowed, an attempt is made here to see if these obscure "spontaneous" neurological phenomena become any more understandable if one simply pictures the central nervous system as a place in which, under certain conditions and in certain areas, excitation waves move along pathways which ultimately return them to their starting points. This possibility is selected because such a circular wave would constitute a source of energy, which under certain conditions would give little or no outward signs of its existence, but which, with a slight change in conditions, might suddenly become manifest. That the nervous system is a "storehouse" of energy in some form is an old and necessary conception. The tacit assumption has been that this is some unknown form of static energy which can on occasion be transformed into nervous impulses and "released." The speculations presented here suggest that these phenomena can all be understood in terms purely of excitation waves and axonal impulses.

This implies that the excitation wave and the axonal impulse are not necessarily identical, a position which Sherrington has also found useful and necessary, and which he has expressed in his surmises about an "excitatory agent." Furthermore, it challenges a too rigid adherence to the neurone doctrine—denying that confidence in the general validity of the doctrine which imposes upon us the belief that no disturbance to the polarity of the neurone or synapse can ever occur, even in abnormal states.

In order to understand how excitation waves which run in closed circuits can affect the surrounding tissues, it is necessary to review their rather peculiar properties. Such a circular wave constitutes a delicately balanced system whose course can be changed, and indeed whose very existence can be terminated by slight changes in the inter-relations of four sensitive factors: (1) the initial intensity of the wave (which for any single pathway in which the All-or-None principle rules will depend upon the state of conductivity of the tissue); (2) the velocity of the wave; (3) the length of the circuit; (4) the duration of the relative or absolute refractory phase which follows the passage of the wave. For instance, if some metabolic change or an alteration in blood-supply or an appropriate drug should lengthen the duration of the absolute refractory period, the wave on its next circuit might reach tissue which was still refractory and through which it could not pass; and thus it would be quite annihilated. The same thing might result from a change in velocity. Or a combination of such changes, even without any alteration in the anatomical organization of the tissue, might simultaneously close a normal pathway and open an unusual one, thus altering the direction and the length of the circuit through which the wave had to pass. And by similar changes not only may closed circuits be converted into open ones, but open circuits may be thrown into new relationships and closed circuits set up. If, therefore, it should prove possible to find any good reason to believe that circular excitation waves exist normally in any parts of the nervous system, it would be possible to use such waves in explaining spontaneous neurological phenomena.

(It may be worth while to recall that just such a system as this is at present supposed by Sir Thomas Lewis and others to provide the mechanism of auricular flutter and fibrillation, the former being due apparently to a stable circus movement over a constant course, and the latter to movements over irregular and varying circuits.)

Where, then, in the nervous system might one look for such pathways? In answering this question it becomes necessary to give to the loosely-used concepts of "active areas" and "silent areas" a quite precise meaning. By "active areas" will be meant all of those structures over which no nervous impulse can pass without producing some bodily change; whereas by "silent areas" will be meant those tissues through which an impulse may pass without reacting upon the rest of the body.

In thinking about the central nervous system, it is customary to assume that all impulses or excitation waves move from some point of origin to some terminus, over pathways all of which lead either INTO or ultimately OUT OF the central nervous system. However complicated such paths may be in detail, all of them are essentially open circuits, like a horse-shoe—with an afferent and an efferent limb. Let us accept this as a true picture for all of those parts of the brain which we ordinarily designate as "active,"—i.e., those which have a direct motor, sensory, or vegetative significance. Roughly speaking, then, throughout this "active" tissue there can be no play of impulses without either visible movement or sensible feeling or some alteration of internal economy. When the body is at rest, the tissues of these active areas of the brain must be at rest. (It is not essential to this reasoning to discuss whether this state of rest is absolute or merely relative, i.e., below a threshold value.)

Within the so-called "silent" areas of the brain, on the contrary, it is possible to imagine a state of constant activity, even when the body is at rest. In fact, it is fairly clear that not only is this possible, but it would seem to be a very probable state of affairs. Furthermore, this activity can be quite plausibly pictured as consisting of innumerable excitation waves circling continually in closed and silent pathways.

The appeal of this concept rests upon the following reasons:—

At every moment the central nervous system is receiving proprioceptive and exteroceptive stimuli in great numbers. To these impulses one of three things may happen: they may pursue an unchecked course from afferent to efferent pathways (i.e., the horse-shoe circuits of the active areas of the brain); or they may enter refractory areas in which they are destroyed; or they may encounter refractory pathways in the active area, but pathways that are open into the silent areas. Once within the silent areas they must either circle until they are destroyed, or ultimately come out again into active efferent expression. On some such basis one may picture the circuits of the silent areas arising. It is equally possible, of course, to postulate the existence of centres which spontaneously generate and discharge impulses within these silent areas. But such a postulate is merely another speculation, and the impulses so generated would also have to meet with one of these three fates. So that it seems to lessen the speculations by at least one hypothesis, to think of the activity in the silent areas as being the result of afferent impulses diverted from the active afferent system into the silent areas and circling there. But whatever their hypothetical origin, the important thing to emphasize is that impulses playing about within the nervous system face one of three possible fates: they must either go in open circuits which must ultimately lead to efferent expression; or they must become annihilated in refractory tissue; or they must wheel in regular or irregular circuits which ultimately bring them back upon themselves. If all three of these things are constantly taking place, it seems plausible to picture the active areas of the brain as areas which are normally organized for straightforward transmission of impulses in well-defined pathways from afferent to efferent aspects of the tissue; whereas the silent areas of the brain may be defined as those tissues which are so organized that stimuli which enter them tend to circle through them in closed circuits. To some extent, and in certain parts, these tissue-types may be organized into macroscopically separate and circumscribed structures. In other regions, the tissues may be so intermingled that they can be recognized only under the microscope as cyto-architectural units.

To these three possible fates one may add one further possibility: that impulses which enter the silent system might engender there the accumulation of some sort of "nervous energy" or excitatory agent, at the same time undergoing extinction themselves. This accumulation of energy could then be looked upon as a potential source of involuntary movements, if its discharge were freed by disease from some normal pattern of regulation and "inhibition." (The word is placed in quotation marks because it implies an entirely new, undemonstrated, and hypothetical kind of "inhibition," which is little more than loosely analogous to the known manifestations of central or peripheral inhibition.) This speculation in some form might be said to be the secret assumption that runs through much current neurological thought. It it no less potent as a speculative assumption merely because it is left unformulated. Indeed, it would seem preferable to make a frank formulation of such an hypothesis, exploring its possibilities and its difficulties fully, instead of allowing it to colour our thinking in silence. The speculations presented in this paper are an alternative hypothesis, an effort to explore possible lines of investigation and explanation without recourse to the notion of the central nervous system as a storehouse of some unknown form of static "nervous energy," but rather as a site of multiple circuits of excitation waves, only some of which are normally in direct connection with the body as a whole.

If they exist at all, there must be countless such circuits; and at any one moment some will be stopping because they are encountering refractory tissue, others starting, still others travelling at diminished intensity through tissue of partial refractivity, &c. And of all of this activity there may be outwardly no normal sign. It is, however, equally possible that the algebraic sum or the distribution of all of this activity may bear some relationship to many states of psychomotor activity—such as sleeping, waking, confusion, alertness, &c. It is attractive to speculate of such possibilities, but quite outside the main purpose of this paper.

On the other hand, it is part of its chief purpose to show how relatively easy it is to understand how such silent circus rhythms could act as a source of spontaneous involuntary movements. It is necessary to imagine only that the normal circuits through a silent area are altered by some pattern of lesions, or that the velocity of the wave or the duration of the refractory period is changed by some toxic or vascular or metabolic factor. As a result, normal pathways might be closed and unusual pathways opened which would lead the circling impulse out of its silent home into one of the active regions. What would happen then would depend upon the nature of the site which was invaded and the conditions met with there; but the passage of the wave through the active area would in each instance result in a discharge along some motor, sensory, or vegetative route. If the new circuit, once established, persisted unaltered—circling with a steady rhythm out of the silent area to touch the active area at a constant and limited point before swinging back again—the phenomenon of rhythmical clonic spasm could be readily understood (fig. 1). But if the circuits through the silent area were inconstant and tortuous, and if the points of escape were more than one, or if the active areas were played upon at more than one locus, the grotesque and irregular phenomena of chorea or athetosis would also seem to be explicable (fig. 2).

One may carry the speculation still further, and imagine that the escaping wave of excitation meets conditions in the active area which are so abnormal that instead of playing over the region merely for an instant it establishes here a temporary circus rhythm (fig. 3). If this occurs in the occipital cortex, is it hard to imagine that the result would be the scintillating phenomena of migraine, whose wheeling lights may be taken as giving support to some of these speculations? Or if certain cell layers of the motor system were involved, might not epilepsy be the expression of the process?

The duration of such a circus movement in an active area might vary from a moment to hours or even days, depending upon the stability of the circus rhythm set up; which—in turn—would depend upon the fundamental variables of wave velocity, circuit length and duration of the refractory phase. An unstable, temporary circus rhythm would correspond to the ordinary isolated epileptic seizure. A more stable system might explain status epilepticus. And it may be that a closer approach to the therapeutic solution of these difficult problems will depend upon the finding of drugs which will alter in the central nervous system the relations of velocity to refractory phase, just as quinidine has been shown to act upon these factors in checking the probable circus movements of auricular fibrillation in heart muscle.

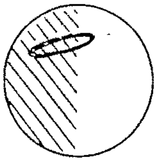


FIG. 1.

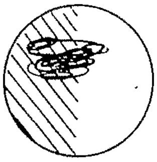


FIG. 2.

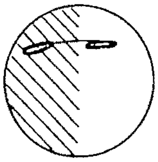


FIG. 3.

FIG. 1.—Circular excitation wave pursuing a regular and constant circuit, escaping from the silent system (shaded) to the active system (unshaded) always at the same point and at a constant rhythm. Such a pathological system could explain rhythmical clonic spasm.

FIG. 2.—Circuitous excitation wave pursuing an irregular and tortuous pathway, and escaping from the silent system (shaded) to the active system (unshaded) at multiple and varying points. Such a pathological system might account for athetosis or chorea.

FIG. 3.—Circular excitation wave escaping from the silent system (shaded) into the active system (unshaded) and setting up a temporary circus movement in the latter. Such an occurrence might underlie the epileptic attack

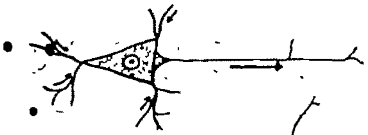
There would seem to be many implications of these speculations for pathology and for experimental physiology. If the speculations represent even an approximation of the true picture, it would no longer seem reasonable to seek for the pathological basis of such symptoms in a single lesion; rather would one expect that similar symptoms could arise from any of several patterns of multiple lesions, the effects of these lesions being influenced in turn by somatic factors which would alter velocity, refractory periods, &c. A reconciliation between the neurogenic and somatogenic explanations of epilepsy might well evolve along these lines.

The immediate need, of course, is for experimental substantiation for these hypothetical closed circuits in the "silent" areas and a more intimate study of conduction of the excitation wave among the neurones of the brain. This presents obvious difficulties because here, as elsewhere, unless discharges proceed synchronously their electrical effects will tend to cancel each other. Such technical difficulties are not, however, insurmountable to modern methods.

It faces us, furthermore, with a fundamental problem as to the rôle which dendrites and neurones may play in conduction of the excitation wave. It is usual to think of the dendrites as the receiving antennæ of the neurone, with the axone as the only efferent channel, and of the nervous impulse as passing from the dendrites directly through the cell body, and out through the axone (see fig. 4). This may be true for the neurones of the active areas of the brain, and perhaps for all. But under abnormal conditions in the active areas, and perhaps even normally in the silent areas, it is possible to visualize the passage of an excitation wave in closed circuits from one neurone to another in one of two ways: either along one of the divisions of a branching axone (as in fig. 5), or along what would ordinarily be called their dendrites (as in fig. 6). In either case, as Sir Charles Sherrington suggests (personal communication), it is the Golgi Type II cell which would seem to lend itself most readily to this type of organization as a normal function. The second alternative, in which the circular excitation wave spreads from neurone to neurone along the dendrites, with effective discharges escaping from the circuit along the axones, involves a much more serious divergence from current assumptions; i.e., it implies that the excitation wave and axonal impulse may not be identical, that not all dendrites are exclusively receptive in function, that it may be possible for an axone to be in a refractory phase while its cell body and dendrites are active, &c. For most types of central neurones there exists no absolute evidence against such possibilities (except perhaps that which can be found in the recent paper of Denny-Brown and Cooper, for the irreversible conduction in the anterior horn cells). Nevertheless, it is probably well to hold this second possibility in reserve as the less likely alternative, depending rather upon the circuit-pattern which makes use of branching axones until such a pattern is shown to be insufficient.

It is possible to imagine that such circus movements might occur abnormally in many regions of the brain and cord, and even in

FIG. 4.



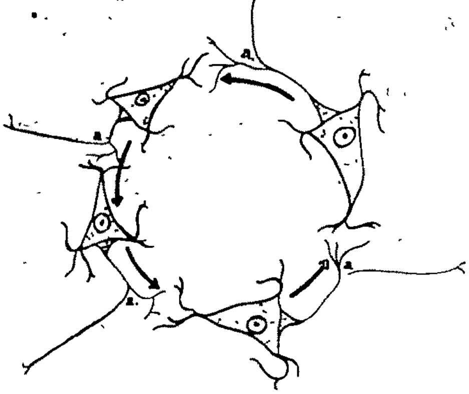


FIG. 5.

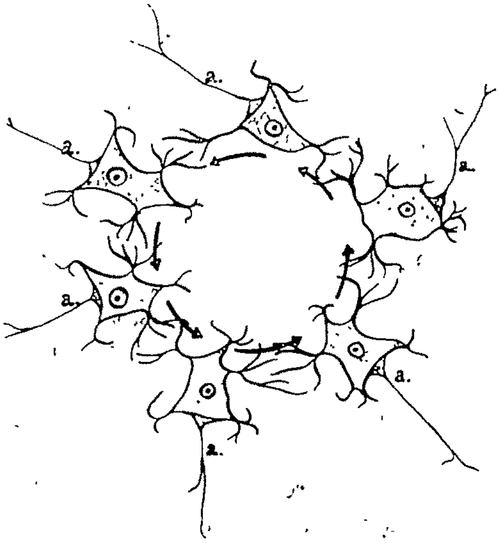


FIG. 6.

FIG. 4.—Accepted picture of conduction of the nervous impulse through the dendrites, cell body, and axone.

FIG. 5.—Diagram of an excitation wave circling through a group of neurones, and following the accepted ideas of conduction through polarised neurones and synapses, i.e., from axone to dendrites or cell body (as in fig. 4). Such a system would affect other regions of the CNS only through the impulses which escaped from the closed circuit along the branching axones (*a*).

FIG. 6.—Diagram of an excitation wave circling through a group of neurones according to a less orthodox pattern of conduction than in fig. 5. Here the wave passes from neurone to neurone along their dendrites, while the axones (*a*) lead out of the circuit and respond to the circling wave of excitation when they are not in a refractory phase. It is less likely that this is a normal form of circuit than that pictured in fig. 5.

sensory or vegetative ganglia. This leads one to wonder what rôle they might play in the production of spontaneous sensations, spontaneous pain, vegetative crises, &c. Nor is it difficult to imagine that they might take part in the production of such sustained disturbances as tremor, myoclonus, and fibrillation.

It is not inconceivable that among certain neurones they may support normal functions. The relatively autonomous rhythm of discharge along post-ganglionic fibres of the sympathetic system is understandable on such a basis. The tetanic nature of the crossed extension response to a single afferent stimulus is not difficult to explain by means of a circus rhythm which repeatedly fires the efferent cells. Even in the phenomena of tonus and tonic perseveration there is room for these speculations. One is tempted, furthermore, to point out that in the production of these phenomena it would make a great difference whether the circling waves were synchronous or asynchronous, rhythmical or arrhythmical (i.e., constant or varying orbits), confined to a group of synergic neurones or traversing the boundaries between antagonistic groups. But perhaps it is better to resist the impulse to exploit the idea any further until some fragments of experimental support should have accumulated.

In conclusion, these speculations may be reduced to a series of propositions.

(1) The brain consists of two types of tissue which can be called respectively the "active" and the "silent" systems of the brain.

(2) To some extent, and in certain parts, these tissue-types may be organized into macroscopically separate and circumscribed structures. In other regions, the tissues may be so intermingled that they can be recognized only under the microscope as cyto-architectural units.

(3) By "active" tissue is meant all of those neurone systems which are so intimately and directly related to the rest of the body, that the passage of an impulse along any of them always registers in some way in the body economy. There can be no play of impulses along the neurones of this active system which is not directly referable to the exterior of the central nervous system, either along afferent or efferent pathways.

(4) The neurones of the active system may be organized, under normal conditions, strictly according to the neurone doctrine, i.e., with dendrites afferent to the cell body and axone efferent from it, and with irreversible synapses. (The possibility must be borne in mind that under abnormal conditions this organization for through-and-through

conduction with irreversible synapses may be altered, and that there may be some departure from this, even normally.)

(5) Under normal conditions impulses impinge upon the active system only or chiefly from stimuli arising from without the central nervous system.

(6) Under abnormal conditions impulses may arise within the active system from stimuli which reach it from the silent system of the brain, causing spontaneous movement and sensation, or spontaneous vegetative alterations.

(7) This necessitates speculation as to what possible sources may exist in the silent system for such an aberrant stimulus:—

> (*a*) The silent tissues of the brain are defined as those through which impulses may pass without any external registration of their passage.
>
> (*b*) Until extinguished by meeting with refractory tissue, such impulses will continue to circulate indefinitely.
>
> (*c*) This implies the existence of circuitous pathways through the silent system—pathways which may be long or short, regular or tortuous, constant or varying—but which must ultimately return upon themselves.
>
> (*d*) Whether the impulses which travel along the pathways of the silent system are produced by some hypothetical form of spontaneous generation of impulses within this system, or whether they result from a diversion of proprioceptive impulses out of the active afferent system into the silent circuits, is immaterial to the main speculation, which is that there is a silent system in which such circling impulses normally exist.
>
> (*e*) Pathological states which divert these silent circling impulses out of their normal silent pathways into the active system offer a plausible explanation of spontaneous sensation or movement, whether the latter be chorea, athetosis, rhythmical clonic spasm, or epilepsy. In the latter, the speculation surmises the establishing of an irregular, transient circus movement in the active motor system.
>
> (*f*) Such pathological states may be a combination of local lesions, or merely a chemical change which alters the relations of conduction velocity, duration of refractory phase, intensity, and the length of the circuit.

(8) These speculations suggest many departures from the tacit assumptions of current neurological thought—departures which imply a somewhat less rigid adherence to the neurone doctrine than is customary,

without, however, demanding that this fruitful doctrine be abandoned *in toto* :—

(*a*) Not all neurones must necessarily be organized for through-and-through conduction, with irreversible synapses. Those of the silent system may be organized for more circuitous and diffuse conduction systems.

(*b*) Even within the active system it is conceivable that conduction in closed circuits may play some normal rôle—and certainly it must be reckoned with as one of the possible explanations of abnormal functions. (This paper has attempted to give illustrations of possible examples of such disturbances.)

(*c*) The excitation wave in dendrite and neurone may not be identical with the axonal impulse, as is usually assumed. The laws of conduction within the neurones of the central nervous system must, therefore, be studied as intensively as has been done in the peripheral axone.

(*d*) The circling excitation wave may be closely related to the excitatory agent which Sherrington has found it necessary to postulate, and inhibition may find its mechanism, as Keith Lucas suggested, in some expression of the refractory phase; to which the suggestion is added here that it may be of the refractory phase, or some other fundamental attribute, of the circling excitation wave.

In reviewing the development of these ideas in my own mind, I find one special indebtedness which I wish to acknowledge. I had for some years been ruminating about what rôle circus movements might play in the central nervous system—thinking especially about such rhythms among the cells of the brain-stem, cord and basal ganglia. In the autumn of 1929 my friend, Dr. Jonas Friedenwald (Ophthalmic Surgeon and Pathologist to the Wilmer Ophthalmological Institute of the Johns Hopkins Hospital) made the observation to me that the wheeling lights of his own migrainous headaches made him think of circus movements in the occipital cortex—and that by analogy epilepsy might be explicable in a similar way. This stimulated me to the present effort; and for the rest of these speculations, as presented here, I must take the blame; except that I acknowledge with gratitude the critical objections and suggestions of Drs. John Fulton, David Rioch, E. G. T. Liddell, and D. Denny-Brown, all of which I have tried to reply to or incorporate here. Finally, it is a pleasure to express my gratitude to Sir Charles Sherrington for his fundamental criticisms and for the encouragement without which I would have hesitated to publish these speculations.

THE INFLUENCE OF EFFERENT CEREBRAL PATHWAYS UPON THE SYMPATHETIC NERVOUS SYSTEM.

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INTRODUCTION.

STUDY of the anatomy and physiology of the autonomic nervous system has always been difficult. From the morphological point of view the peripheral nerves and ganglia are diffuse and do not lend themselves, as a whole, to satisfactory macroscopic or microscopic examination. Knowledge of the physiology of the autonomic system has been illuminated by the discovery that certain drugs have specific action upon its activity.

Certain data concerning the general plan of the peripheral autonomic reflex arc are now available. Small motor cells found in certain parts of the brain-stem and cord give rise to the preganglionic neurones which connect in the periphery of the body with the postganglionic neurones. Afferent impulses are carried from the structures innervated by the autonomic fibres to the central nervous system and are supposed to influence the reflex activity of the motor cells.

There is much less information concerning the control of this primary reflex arc by the higher correlation centres of the brain. It has become clear, however, that abnormalities of the structures in the floor of the third ventricle, following invasion by tumours or injury in lethargic encephalitis, for example, cause metabolic disturbances influencing weight, sleep, fluid intake and output, vasomotor control and sweating. The conclusion, therefore, seemed justified that groups of cells in this area form a general central controlling centre for autonomic activities.

The pathways that carry the impulses from centres in the hypothalamus to the preganglionic autonomic cells of the brain-stem and cord have never been clearly demonstrated. These pathways are non-medullated and are believed to consist of chains of neurones with numerous synaptic junctions.

The present paper attempts to determine some of the influences from the brain that control the primary autonomic reflex arcs. The experiments recorded here have to do only with the phenomenon of sweating. Therefore specific attempts to study the cerebral control of the autonomic system will be recorded only inasmuch as they have to do with sweating. Moreover, stimulation of the sweat-glands is a function of only one group of cells of the autonomic system, the sympathetic cells of Langley's classification.

A.—PREVIOUS STUDIES OF THE CEREBRAL CONTROL OF SWEATING.

Bechterew (1905 and 1911) found that faradic stimulation of certain areas in the anterior portion of the cerebral cortex, close to the motor area, in cats produced sweating of the foot-pads which could be demonstrated on inspection and with the use of litmus paper. The secretion occurred in all four extremities, although it was more marked in the extremities of the opposite side. A diagram (1911) shows the exact position of the two circumscribed cerebral areas from which this phenomenon was obtained. If these areas be projected upon the drawing of the cerebral cortex of the cat in the present paper (fig. 1), one corresponds to areas A and G and the other to area D. Bechterew pointed out that sweating was a frequent accompaniment of mental activities, particularly under certain pathological circumstances. He also collected cases in which sweating of the opposite side of the body was associated in man with glial tumours infiltrating the frontal lobe and encroaching on the motor cortex.

Winkler (1908), working with the cat, confirmed these observations of Bechterew. He, moreover, exposed the floor of the fourth ventricle and obtained profuse sweating of the foot-pads of all four feet on faradic stimulation of an area one millimetre cephalad to the calamus scriptorius. Faradic stimulation of the cerebral peduncles also elicited sweating of the foot-pads.

Karplus and Kreidle (1909) demonstrated that stimulation of the tuber cinereum, behind the optic tract and lateral to the infundibulum, elicited, in the cat, dilation of the pupils, retraction of the nictitating membranes, secretion of tears, a rise in the general arterial blood-pressure, and profuse sweating of the pads of all the feet. They assumed, without any adequate reasons, that they stimulated the subthalamic nucleus and thought this nucleus was of autonomic function.

In all of these experiments the effect on sweating produced by faradic stimulation of the cortex or brain-stem was judged either by the presence of visible sweat or by changes in the litmus paper applied to the skin. These criteria have obvious limitations. In the first place a fairly strong and continuous stimulation is necessary to produce visible sweat, and then the sweat must be wiped off before each repetition of the stimulation. This method does not permit of an actual measurement of the effects produced by the stimulus, nor of photographic registration of the types of response.

B.—A Delicate Method of Recording the Activity of the Sweat-glands on the Foot-pads of Cats.

Through the galvanic skin response method of studying the activity of the sweat-glands most of these limitations are overcome. By this method the activity of the sweat-glands is measured indirectly through the action currents given off from the glands when they are activated. The close correspondence between activity of the sweat-glands and the galvanic skin response has recently been clearly demonstrated by Darrow (1927). The extraordinary degree of sensitivity of this method can be seen by the fact that even a slight emotional or nocuous stimulation in an intact animal or in man is sufficient to cause a galvanic current to be given off by the sweat-glands. Also, a small make and break shock applied to the sympathetic chain or to the base of the brain produces a definite galvanic skin response (Wang and Richter, 1928).

The technique of obtaining this reflex has been described in detail in previous papers (Richter, 1927, 1928, 1929 and 1930). Only a brief description of the essentials will be given here. The electrodes, zinc discs and kaolin paste, are attached to the skin on the large central pad of the foot and to the pinna of one ear, the skin of which had previously been pierced with a hypodermic needle. In this way responses from the ear are eliminated and only the responses from the pad of the foot are obtained.

The electrodes on the pad of the foot and the ear are connected to a string galvanometer of the same type used in cardiac departments. No external current is employed, so the currents that are given off have their origin in the sweat-gland activity in the skin of the pad of the foot. Two records of the galvanic skin response produced by stimulation of the brain-stem and cortex are shown in fig. 15. Time in seconds is indicated at the top of the records, the incidence of the stimulus (faradic current) at the bottom, and the galvanic current in the middle. It may be noted that the latency of the responses is about one second, which clearly distinguishes them from muscular responses. These records will be discussed again below.

C.—The Location of the Motor Cerebral Cortex of the Cat.

In recent experiments (Weed and Langworthy, 1926, and Langworthy, 1927) attempts have been made to map out the motor cerebral cortex of the cat by the method of faradic stimulation, and also to follow the development of responses from the motor cortex in young kittens. The results may be interpreted by consulting fig. 1. Stimulation of areas A and B produced flexion of the contralateral fore-leg, of areas E and F flexion of the contralateral hind-leg, while stimulation of area C elicited contraction of the facial and masticatory muscles of the opposite side. No motor response was ever obtained on stimulation of area D.

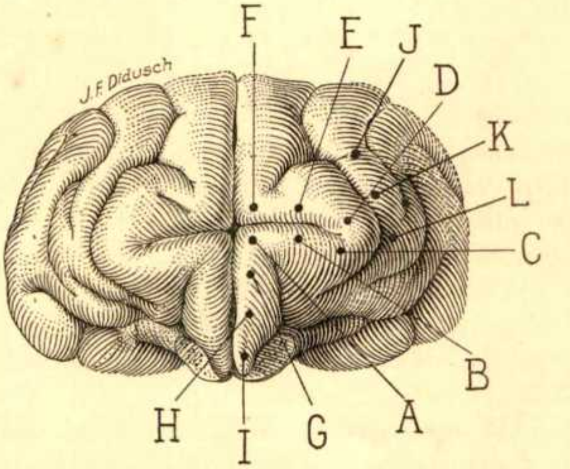


Fig. 1.—Frontal view of the cerebral cortex of the cat. Galvanic skin responses were obtained on faradic stimulation of areas A and G and areas D and K. Contraction of the contralateral somatic musculature was elicited from areas A, B, C, E and F.

Afterwards it was shown that removal of the area frontalis, including areas A, G, H, and I of fig. 1, produced abnormalities in tonus of the contralateral legs, manifest as hypertonus (King, 1927, and Langworthy, 1928). It was suggested that the fronto-ponto-cerebellar tract arises from cells in this area and abnormalities in tonus occur as a release phenomenon after its injury.

It was possible to use this previous work as a basis for studying areas in the cerebral cortex from which the action currents could be demonstrated after faradic stimulation, and to correlate the location of these new areas with those to which attention had already been directed.

METHODS.

An attempt was made in this study to survey the cerebral cortex and brain-stem for areas from which activity of the sweat-glands could be elicited by Faradic stimulation. Thirty-six cats were used in these experiments. The cat was given ether at the beginning of the experiment and remained under the anæsthetic until after decerebration. Inasmuch as decerebrated cats no longer are conscious or feel pain, the ether was discontinued. Artificial respiration by a tracheal tube was used when sections of the lower brain-stem were made. In many cases the carotid arteries were tied to limit the bleeding; pressure on the vertebrals also helped to control the hæmorrhage.

At the beginning of the experiment the cerebral cortex was exposed on each side. Stimulation of the cortex was not confined to the region of the motor area, but the whole dorso-lateral surface of both hemispheres was explored. After the results from the intact cortex had been ascertained, transections of the brain were made with a sharp knife. These sections were not exactly coronal but sloped in an anterior direction towards the ventral surface. After bleeding had been controlled, the whole cut surface was carefully explored with the stigmatic electrode. In each animal three or four of these transverse sections were studied successively before the tentorium was reached. At this point the tentorium was cut away and the bone removed from the whole dorsal surface of the cerebellum. After faradic exploration of the dorsal surface of the cerebellum, the cerebellum was removed entire by severing the peduncles. This exposed the whole floor of the fourth ventricle which was explored for areas from which galvanic skin responses could be obtained. Areas which gave a response are shown in fig. 2 (areas 1 and 2).

The lower portion of the brain-stem was now exposed, permitting further transverse sections. Artificial respiration gave proper oxidation of the blood and the animals remained reflexly responsive. It was possible to continue the study of transverse sections into the region of the cervical cord.

A faradic current from an induction coil was used for stimulation of the central nervous system. A large indifferent electrode was attached to the back of the animal. The stigmatic, stimulation electrode consisted of a fine platinum point mounted on a delicate spring. It could be demonstrated that relatively little spread of the current occurred around the point of stimulation. The strength of current necessary to obtain the reflex was approximately the same as that required to elicit a motor response. In several instances it was much smaller.

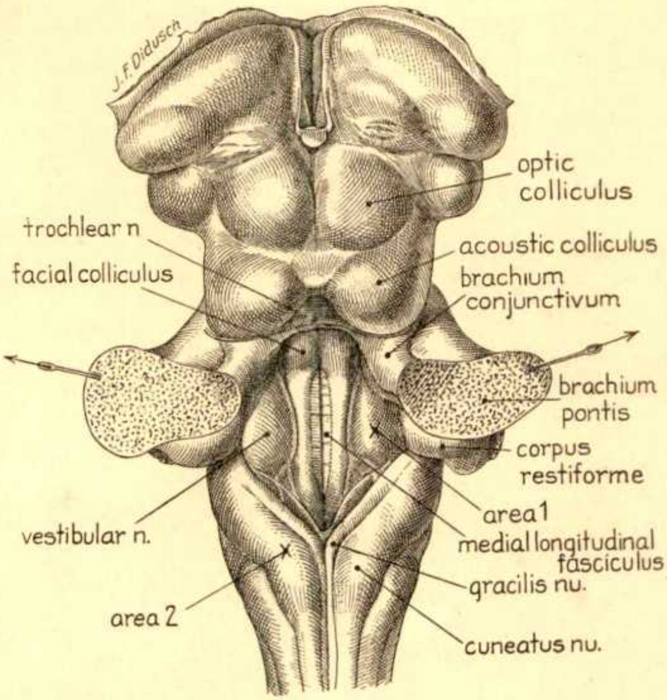


FIG. 2.—Drawing of the floor of the fourth ventricle of the cat. Galvanic skin responses were obtained from the region of the vestibular nuclei (area 1) and from the posterior column nuclei (area 2).

EXPERIMENTAL OBSERVATIONS.

A general survey of the central nervous system was made for groups of cells or tracts of fibres from which responses could be elicited on faradic stimulation. The results may be described under a number of headings.

(*a*) *Stimulation of the Cerebral Cortex.*

The whole dorso-lateral surface of the cerebral cortices was explored with the stigmatic electrode for areas from which stimulation of the sweat-glands could be obtained on stimulation. The two areas that gave autonomic responses were sharply circumscribed and were adjacent to the motor cortex from which contraction of the contralateral musculature may be obtained. They corresponded almost exactly to the areas previously described by Bechterew. One of these areas was anterio-medial to the motor cortex, occupying areas A and G of fig. 1. The maximum response was obtained in the boundary between areas A and G. The second area was just posterio-lateral to the motor area, which gives responses of the contralateral striated musculature. It occupied areas D and K of the diagram (fig. 1), with the maximal response from area K. No action current was obtained on stimulation of any other portions of the cortex.

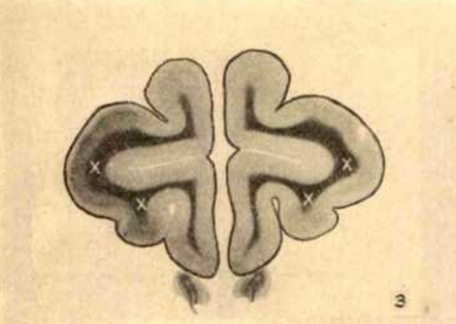
As has been described, the responses were recorded quantitatively in terms of deflection of the galvanometer string. Approximately equal responses were obtained from these two areas. On stimulation of one of these points in one hemisphere, action currents could be obtained from all four legs, although they were more marked on the contralateral side. The fore-legs gave more marked responses than the hind-legs.

Before attempting to follow tracts from these areas from experimental level to level of the brain-stem, it is important to seek some interpretration of the possible connections of these areas. As already suggested, there is some evidence that areas A and G give rise to the cortico-pontine fibres, influencing the tone of the striated musculature through the cerebellum. This pathway lies mesial to the cortico-spinal tract in the internal capsule. A temporo-pontine tract descends just lateral to the cortico-spinal fibres to connect with the cerebellum in a similar way. It may be said that areas D and K give rise to the temporo-pontine fibres.

(*b*) *Faradic Stimulation at Different Experimental Levels of the Fore-brain.*

The areas from which galvanic skin responses were elicited from transverse sections of the fore-brain are shown in figs. 3 to 7. The first section (fig. 3) is just caudal to the motor area. Two circumscribed points were constantly localized in each hemisphere; responses could be obtained from each of them. Their relation to the cortico-spinal tract becomes clear if they are followed in figs. 4, 5 and 6. It is evident that one group of fibres lies mesial, the other lateral to the cortico-spinal tract. This again suggests that they are fronto- and temporo-pontine tracts. They may be followed into the region of the mid-brain where all three cortico-efferent tracts become extremely compact (fig. 8) and can no longer be differentiated by faradic excitation.

At the levels of the fore-brain corresponding to figs. 3 and 4, the only responses were from areas that corresponded with tracts from the cortical areas already described. Other responsive points appear in figs. 5, 6, and 7. A group of these points lies near the ventral mid-line, around and in the floor of the third ventricle. In fig. 5 the third ventricle is a narrow median slit; this section is anterior to the optic chiasma which is seen in fig. 6. Just lateral to the third ventricle and ventral to it galvanic skin responses were obtained on stimulation. The area just ventral to the optic chiasma was responsive in fig. 6; also an area in the mesial portion of the thalamus and the region of the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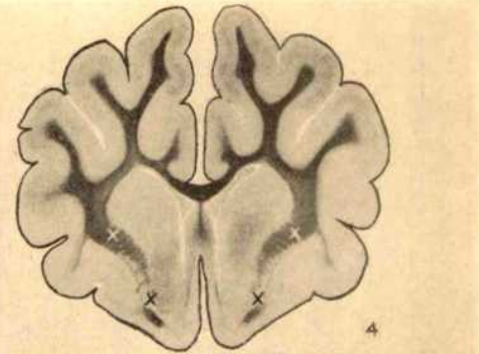
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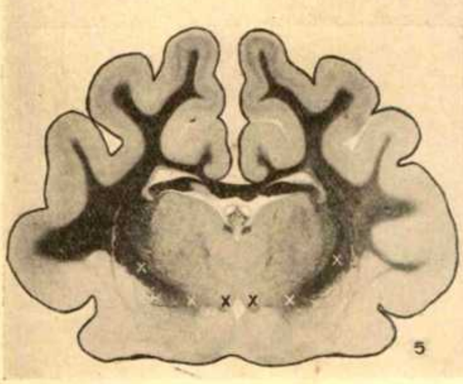
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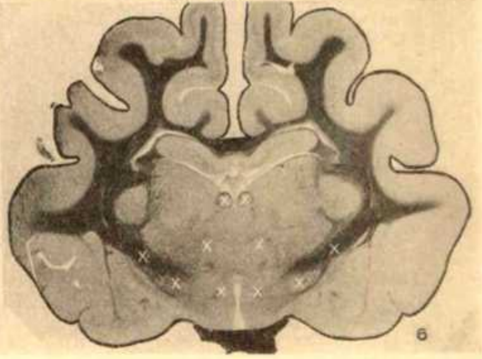
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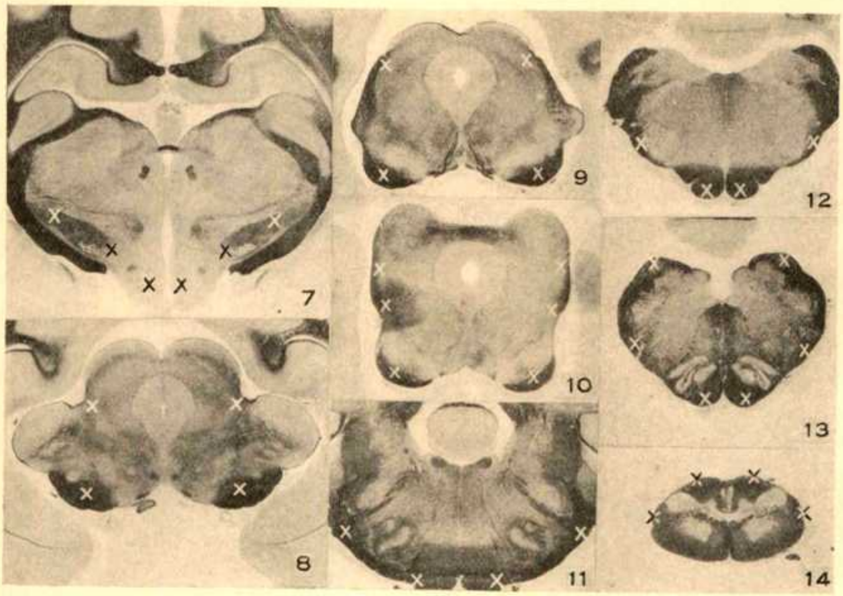
habenular nuclei at the dorso-medial edge of the thalamus. In fig. 7 a responsive area in the tuber cinereum is charted.

The ventral or hypothalamic area from which responses were obtained includes the whole tuber cinereum region. This area lies just between the cerebral peduncles, and the question may be raised as to whether the effects obtained were not due to spread of current into the tracts that have been followed from the cerebral hemispheres. Against this view is the fact that large deflections of the string were elicited from the tuber cinereum, greater than from the region of the cerebral peduncles. There are, then, groups of cells in the tuber cinereum which, on stimulation, produce sweating of the foot-pads.



FIGS. 3 to 14 are photographs of coronal sections of the brain of the cat stained by the Weigert-Pal method. The areas which gave galvanic skin responses on faradic stimulation are indicated. A discussion of these areas will be found in the text.

Nothing more need be said here concerning the areas in the thalamus and habenular nuclei from which action currents were obtained. These will be discussed later.

(c) *Galvanic Skin Responses obtained on Stimulation of Transverse Sections of the Mid-brain.*

Three figures demonstrate typical transverse sections of this region; fig. 8 from the extreme cephalic end of the mid-brain, fig. 9 through the optic colliculi, and fig. 10 through the acoustic colliculi. In each case stimulation of the cerebral peduncles on the ventral surface of the sections gave a marked response. Due to the condensation of fibres in this area, the two separate pathways from the cerebral cortex can no longer be differentiated.

In figs. 8 and 9 it will be observed that a galvanic skin response was always obtained from an area on the lateral edge of the brain-stem just ventral to the optic colliculi. This pathway may be followed into fig. 10, where it forms the most dorsal area from which responses were obtained. It could not be followed further caudad in the brain-stem. The connections of this tract are not clear.

Fig. 9 is at the level of the red nucleus. Stimulation of the red nucleus never elicited action currents. The rubro-spinal tracts below this level, however, always gave a marked response on stimulation. This response was more marked than that obtained from the cortico-spinal fibres in the medulla. Thus the lateral area in fig. 10, between the dorsal and ventral points already discussed in the two preceding paragraphs, gave a marked response. This same area can be traced caudad in the other sections (figs. 12 to 14).

(*d*) *Galvanic Skin Responses obtained on Stimulation of the Floor of the Fourth Ventricle.*

After the cat was decerebrated by a transverse section through the mid-brain, the dorsal surface of the cerebellum was exposed. No response was ever obtained on stimulation of the cortex of the vermis or hemispheres of the cerebellum. The cerebellum was then removed in one piece by cutting the peduncles and the floor of the fourth ventricle exposed to view.

Stimulation of the floor of the fourth ventricle and its environs gave marked galvanic skin responses, and confirmed and amplified the findings previously made by Winkler. The responsive areas are indicated in fig. 2 (areas 1 and 2). No response was obtained from the cephalic portion of the floor of the ventricle, from the region of the facial colliculi, caudal end of the aqueduct, or from the dorsal surface of the acoustic and optic colliculi. From an area just medial and caudal to the cut cerebellar peduncles responses were obtained on faradic stimulation (area 1). These bilateral responsive areas include lateral prominences at the widest point of the fourth ventricle. They are the vestibular nuclei which give rise to the vestibulo-spinal tracts and certain fibres running caudal in the medial longitudinal fasciculus.

The most marked action currents obtained anywhere were elicited from the region of the nuclei gracilis and cuneatus just lateral to the caudal portion of the fourth ventricle (area 2). In certain of the cats, relatively unresponsive to stimulation of other portions of the brain, galvanic skin responses were always obtained from these areas. This marked response was obtained, not only from the posterior column nuclei, but also from the surface of the posterior columns throughout the cervical cord.

Between the vestibular nuclei and the posterior column nuclei there was always an area unresponsive to stimulation. No responses were obtained from the medial portion of the floor of the fourth ventricle.

(e) *Galvanic Skin Responses obtained on Faradic Stimulation of Transverse Sections of the Medulla.*

Three typical sections of the medulla are shown in figs. 11, 12 and 13. The ventral areas in each section from which responses were obtained correspond to the location of the cortico-spinal tracts. More marked responses were always obtained from a lateral area marked in each section which corresponds to the region of the rubro-spinal tract.

A third area is marked in fig. 13; maximal responses were always obtained from this region of the posterior column nuclei. This has already been discussed in connection with the surface study of the region of the fourth ventricle floor.

(f) *Galvanic Skin Responses obtained on Faradic Stimulation of Transverse Sections of the Upper Cervical Cord.*

Marked responses were obtained on faradic stimulation of transverse sections of the upper cervical cord. These may be described in connection with a section at the highest cervical level (fig. 14). In the cat the rubro-spinal and cortico-spinal fibres all run in the lateral columns; they are more or less intermingled there. Galvanic skin reflexes were obtained from faradic stimulation of the lateral columns in the region of the cortico-spinal and rubro-spinal pathways. The most marked responses, however, were always obtained from the posterior columns. No deflection of the galvanometer string was ever obtained from the ventral columns.

DISCUSSION.

Certain conclusions concerning cerebral influences upon the preganglionic sympathetic cells of the cord may be drawn from these experiments. It is evident that stimulation of the cortico-spinal, cortico-pontine, rubro-spinal and vestibulo-spinal tracts elicit action currents indicating stimulation of the sweat-glands. It appears, therefore, that the efferent pathways from the brain influence the activity of the autonomic cells in the anterior grey matter of the cord.

This is not a strange, nor should it be an unexpected finding. For many years it has been known that many efferent pathways from the brain influence the somatic motor anterior horn cells, and modern physiological studies give certain clear ideas concerning their functions. Efferent pathways to the cord from the medulla control the tonic patterns of the striated musculature of the extremities in reference to stimulation of the vestibular and optic reflex centres. The cortico-spinal pathway initiates delicate phasic movements, while at the same time there is reason to believe that the cortico-pontine influences inhibit the tonus of the antagonistic group of muscles to make these movements possible. The sympathetic cells lie close to the somatic motor cells in the anterior columns of the cord, so it is not surprising to find that they should be activated by the same cerebral influences. This seems the more comprehensible inasmuch as no cerebro-spinal pathways ending exclusively around the sympathetic cells are known.

The influences of cerebro-spinal pathways upon the somatic motor cells of the cord are probably summated to produce either excitation or inhibition of the activity of the anterior horn cells, which in turn control the tonus and contraction of the somatic musculature of the body. It is important to learn whether evidence of excitation and inhibition can be obtained by recording the action currents in the case of the sympathetic cells of the cord.

Galvanic skin responses similar to those described in this paper may be obtained from normal men and from intact animals with the proper stimulus. For example, firing a pistol close to the human subject will elicit such a response. In man, a response is obtained by reading a list of words, some of them giving strong emotional reactions. The galvanic skin reflexes obtained under these conditions are usually biphasic, consisting of both a positive and negative phase. In the present experiments biphasic currents were obtained in almost all of the animals on stimulation of the cerebral cortex; responses from other areas in the brain were uniphasic, of only a negative phase. Records are shown in fig. 15 of the biphasic responses obtained from cortical stimulation and the monophasic responses from subcortical stimulation. This question of positive and negative responses will be studied further.

There is good evidence, however, that the cerebral control of the autonomic system is predominantly an inhibiting one. Riddoch (1917) and Head and Riddoch (1917) had a unique opportunity to study selected cases of complete transverse section of the spinal cord in young human adults, otherwise healthy, in whom the injuries were produced by war wounds which healed rapidly with little infection.

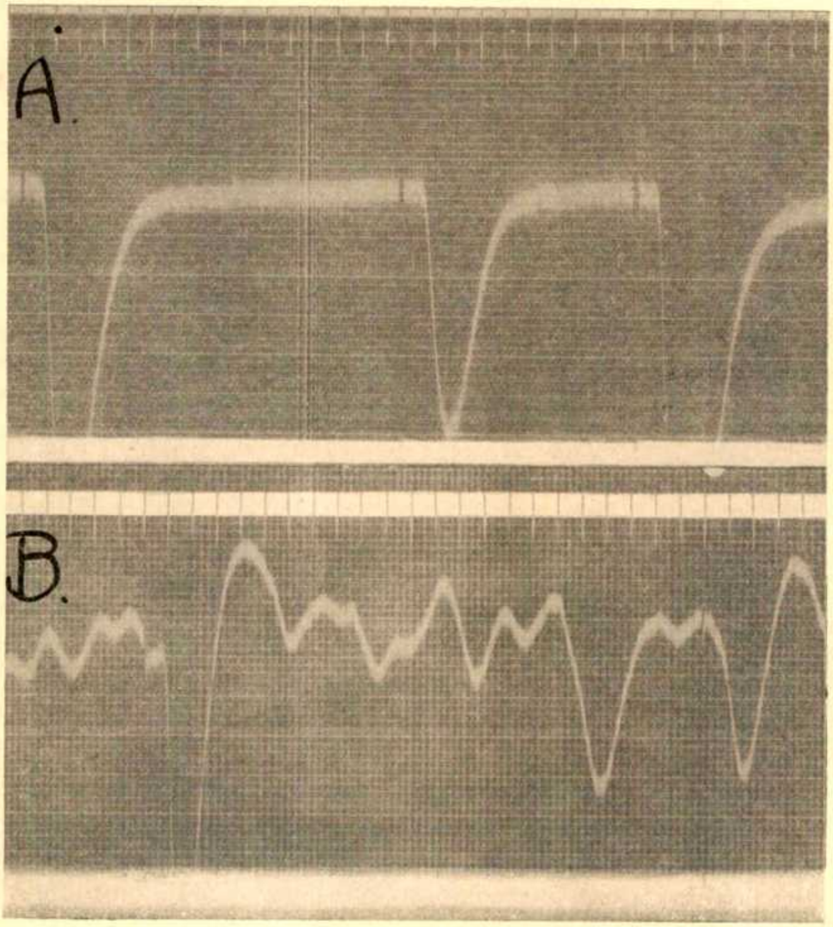


FIG. 15.—Typical galvanic skin responses obtained on faradic stimulation of the cerebrum of the cat. A monophasic response (*a*) and a biphasic response (*b*) are shown. Biphasic responses were obtained on appropriate stimulation of the cerebral cortex. After removal of the responsive areas in the cerebral cortex, monophasic responses were obtained.

For several days following the injury the musculature innervated by the cord below the level of the lesion was completely atonic and no reflexes could be obtained. Similarly, the smooth muscle of the bladder lost its tone. The skin at this time was very dry and no sweating occurred. After a variable period of seven days or more after the injury, reflexes began to return in the lower portion of the body, and later the reflexes presided over by the cord below the lesion became hyperactive. At this time stimulation of the skin produced not only a local contraction of the musculature, but violent mass contraction of all the striated musculature, evacuation of the bladder and sweating over the portion of the body innervated below the lesion. Riddoch pointed out that the reflex arcs lost their local sign and a mass reflex resulted. The profuse sweating indicated that the sympathetic cells of the cord, freed from normal cerebral inhibitory control, became hyperactive.

Richter (1930) has recently demonstrated in animals that the skin resistance is greatly increased and the galvanic skin reflex is absent after transection of the cord in the upper thoracic region for the first few days following the operation. This is the period of spinal shock described by Riddoch in man. Later, when reflexes return and become hyperactive in the posterior portion of the body, the skin resistance drops to normal, or below normal, and the galvanic skin reflex becomes hyperactive, indicating the marked activity of the sweat-glands.

It is clear, then, that following transverse section of the cord, after the period of shock has passed, reflex activity of the autonomic, as well as of the somatic, motor cells becomes greater than normal. This suggests that the cerebral control of autonomic activity in the cord is predominantly an inhibitory one.

In the present experiments responses were obtained from areas in the floor of the third ventricle, from the habenular nucleus and from a mesial area in the thalamus. It is impossible to suggest the anatomical pathways that would carry impulses from these regions to the motor cells in the cord. The reflex path probably connects with cerebro-efferent pathways lower in the brain-stem, the rubro-spinal tract for example.

The most marked galvanic skin reactions were obtained on stimulation of the posterior column nuclei and the posterior columns of the cord. These fibres must make important reflex connections with the sympathetic cells of the thoracic cord.

It seems likely that the two areas in the cerebral cortex from which galvanic skin responses were obtained corresponded to the regions giving rise to the fronto- and temporo-pontine tracts. One area, the frontal, lies just antero-mesial to the true motor cortex; the temporal, postero-lateral to it. There has been previous evidence that the anterior area gives rise to the fronto-pontine tract (Langworthy, 1928). Although these pathways connect with the cerebellum, no action currents were obtained on stimulation of the cerebellar cortex. Stimulation of the related rubro-spinal tracts gave marked reactions.

The galvanic skin responses obtained were always larger from the fore-legs than from the hind-legs. Although the responses were always bilateral, they were usually unequal on the two sides. Those from the cortico-spinal tract were predominantly bilateral, from the rubro-spinal tract and floor of the third ventricle predominantly unilateral.

The responsiveness of the cats varied considerably. A few gave no response at all; others gave only small responses. The impression was gained that the reflex was practically abolished in a period of very deep anæsthesia. The sensitivity of the response could be heightened by keeping the animals in a hot-air bath for several hours before the experiment.

Finally, the conclusion seems justified that the same pathways from the cerebrum that influence and control the somatic motor primary reflex arcs also influence and control the primary sympathetic reflex arcs. Although there may be higher centres for sympathetic control in the brain, these finally exert their influences through the pathways described in this paper. It is clear from observations upon man and animals after complete transection of the cord that this influence must be predominantly an inhibitory one.

SUMMARY.

Using the galvanic skin response as a measure of sweat-gland activity, the controlling influences from the cortex, brain-stem and spinal cord were investigated. Definite galvanic skin responses were obtained from faradic stimulation of two areas adjacent to the motor cortex, from the floor of the third ventricle, from the cortico-spinal and rubro-spinal tracts, from the vestibular nuclei, from the posterior column nuclei and from the posterior columns of the cervical cord.

It is concluded that the same cerebro-efferent pathways which influence somatic motor cells also control preganglionic sympathetic cells; this cerebral control is predominantly an inhibitory one. Any cerebral centres influencing lower centres seem to exert final control through well-known cerebro-efferent pathways.

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A CLINICAL STUDY OF TUMOURS INVOLVING THE OCCIPITAL LOBE.

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I.—Introduction.

Contributions to the literature of tumours of the occipital lobe have been very few, especially during the last ten years. They have been confined to an occasional case report and to two extensive papers—the first by Puusepp [22], not available to the majority of readers, and the second by Frazier and Waggoner [9], as yet available only in abstract. The former paper was based on a series of eight cases, and the latter on a series of forty cases, in nine of which the tumour had originated in the temporal lobe or had invaded the occipital lobe from its origin in the parietal lobe.

It has been thought necessary, therefore, to review the clinical features of a series of tumours of the occipital lobe, and to consider particularly certain points connected with the variations in the visual fields.

This paper is based on material from the National Hospital, Queen Square, London. The writer wishes to take this opportunity of expressing his thanks to the Medical Committee of the Hospital for permission to make use of the material and to members of the Staff for permission to quote cases under their care.

The limitations to be placed upon the choice of cases for study demanded some consideration, and eventually it was decided to base the review on a series of forty cases, the sole condition on which the cases were to be included in the series being that the tumour should have been proved anatomically to have involved the occipital lobe.

A further point for consideration was whether the series should be confined to those cases in which the occipital lobe alone was involved during the whole of the clinical course. A preliminary survey of the material showed that this course was undesirable if a complete account of the clinical features of occipital tumours was to be given. The importance of neighbourhood symptoms and signs was at once evident, so it was found necessary to include in the series for study those cases of cerebral tumour which involved the occipital lobe either primarily or chiefly, whether confined to the occipital lobe or involving other structures as well.

Of the series of forty cases of tumour of the occipital lobe studied, in twenty-four the tumour was entirely confined to that lobe, in six it involved the posterior part of the temporal lobe as well, while in ten it apparently affected a portion of the parietal lobe in addition to the occipital lobe.

It was felt to be inadvisable, on the limited clinical material available, to classify the clinical features according to the position of the tumour in the occipital lobe, as thereby a false impression might be created as to the relative importance of the different clinical pictures. This aspect of the subject will, however, be considered in the discussion of the individual symptoms and in the general discussion of the clinical features later in this paper.

Tumours involving the occipital lobe are relatively uncommon. Dowman and Smith [7] mentioned only two cases in a series of 100 verified intracranial tumours reviewed by them. The incidence of such tumours at the National Hospital during the past ten years has been practically the same or perhaps a little lower. In his review of a year's work at Cushing's Clinic, Cairns [3] mentioned nine cases as having been found in the group of 162 intracranial tumours verified either at operation or at autopsy.

In spite of their comparative infrequency tumours of the occipital lobe are of considerable importance clinically, not only because of the need to localize and deal with them satisfactorily, but also in the differential diagnosis of parietal, temporal, suprachiasmal, cerebello-pontine angle and cerebellar tumours, and of vascular conditions involving the occipital lobe.

The nature of the tumours in the series studied was as follows: In sixteen cases some form of glioma was present, in one an angioma, in three a sarcoma, in two each a gumma and a cyst, and in four an endothelioma. In the remaining cases the nature of the tumour was not recorded.

II.—REVIEW OF THE LITERATURE.

The first reference in the modern literature to the clinical features associated with a lesion of the occipital lobe other than those due to a vascular condition was that of Levick [18] in 1866, who described a patient with left homonymous hemianopia due to an abscess about 1½ in. in diameter on the convex surface of the right occipital lobe. Subsequently, Jastrowitz [16] reported a case of sarcoma of the left occipital lobe involving all three of the convolutions and the precuneus, and associated with a wedge-shaped area of softening passing through the white substance to the posterior cornu of the lateral ventricle. In addition to vertigo, loss of memory and partial agraphia with transient right hemiplegia, the patient had right homonymous hemianopia with preservation of central vision in both eyes. At the same time Jany [14] reported a case of cystic glioma in the left occipital lobe, which had destroyed the cortex of the lobe at its apex and also the entire inner half of the lobe. This patient also had right homonymous hemianopia with preservation of central vision. Traube [28] described a cyst the size of an apple in the white matter of the right occipital lobe in a patient who had had epileptic attacks for seven years, with later an aura of darkness coming over the visual field from the left side. Haab [10] also described two cases. The first was that of a tumour of the inner surface of the apex of the right occipital lobe. There was a zone of yellow softening limited to the cortex. The patient had been irritable and stupid, for two months had had general convulsions, and on examination was found to have left homonymous hemianopia. In the second patient there was a cyst surrounded by an area of softening, 6 cm. by 3 cm., on the inner surface of the apex of the right occipital lobe. There was left homonymous hemianopia, the field of vision in both eyes being limited by a vertical line passing through the fixation point.

Hale-White [11] surveyed the pathological material of Guy's Hospital for the years 1872-1884 inclusive, and found an incidence of one cerebral tumour to every 59·1 cases coming to autopsy. Among the 100 cases of cerebral tumour discussed there were six in which the tumour involved the occipital lobe. Of these two were secondary to tumours elsewhere in the body and two were associated with tumours in other parts of the brain. Insufficient clinical data were recorded for these cases to be of any value in discussion.

Starr [25] discussed the visual area of the brain as determined by a study of hemianopia, and quoted from the literature a series of cases of occipital tumour, including those of Jastrowitz, which involved the cortex of the calcarine fissure either alone or with destruction of other parts of the occipital lobe.

Harris [12] discussed hemianopia with special reference to its transient varieties and considered hallucinations, both of the formed and unformed type, occurring in the hemianopic fields of vision.

In a discussion on the localisation of intracranial tumours, Bramwell recorded the details of four cases of tumour of the occipital lobes, all of them of considerable interest in connection with the more unusual manifestations of tumours in that region. In one case the tumour was confined to the occipital lobe, and in the other three the occipital lobe was affected in addition to other parts of the brain. In the first case a small tubercle at the tip of the left occipital pole produced no physical signs during life. In the second case a large glioma involved and destroyed the greater part of the left frontal, temporal and occipital lobes. Partial right homonymous hemianopia was present early in the course of the case. In the third case a gumma was situated on the outer surface of the posterior part of the left occipital lobe. For fifteen years the patient had suffered from epilepsy with an aura of flashes of light before the right eye and followed by blurring of vision for some days. In the fourth case a nodule the size of a large walnut was found on the outer surface of the left occipital lobe just above the pole, with only slight infiltration of the underlying white matter. Fifty times a day the patient had paroxysmal attacks of headache with flashes of light before the right eye, varying in size from that of a button to that of a large globe. This series of cases illustrated the occurrence of tumours of the occipital lobe with partial homonymous hemianopia and without any changes in the visual fields.

Duret [8] discussed the clinical manifestations of tumours of the occipital lobe in detail and classified the clinical features of the condition into four distinct groups. His first group was characterized chiefly by contralateral homonymous hemianopia, in illustration of which were quoted cases reported by Seguin [24], Schoenborn and Weber. In Seguin's case left homonymous hemianopia was the only sign of a tubercle, 2 cm. in diameter, on the calcarine fissure of the right occipital lobe. Schoenborn's case was characterized by crises of headache, impairment of vision and left homonymous hemianopia in association with a cystic sarcoma of the cuneus, precuneus and neighbouring occipital convolutions. On the other hand, Weber's case of sarcoma of the lingual and fusiform lobes was associated with homonymous hemianopia alone. Duret's second group included those cases of tumour of the occipital lobe which were characterized by hemianopia, hemiplegia and hemianæsthesia; and was made up of tumours of the inner surface of the occipital lobe penetrating deeply, those of the white matter and those occupying the occipital horn of the lateral ventricle. According to Duret, these physical signs were due to involvement of the adjacent sensory and motor paths in the internal capsule. He quoted cases reported by Jastrowitz, Deschefelder, Jany, Lafforgue, Wordsworth and Spiller in support of his conclusion. His third group consisted of those cases in which homonymous hemianopia was associated with sensory aphasia—word blindness, psychic blindness, agraphia and partial motor aphasia. Duret's fourth group was made up of large tumours which produced all the physical signs mentioned above, and sometimes ocular and facial paralysis in addition.

McKennan [19] described the clinical features of a cyst which approached the outer surface of the right occipital lobe close to the pole. In addition to a history of impairment of health and of epileptiform attacks beginning in the left leg, the patient suffered from word blindness and had left homonymous hemianopia with preservation of central vision for 5° from the fixation point. McKennan summarized the diagnosis, pathological features and results of twenty-four cases of tumour of the occipital lobe which had been reported in the literature, but did not discuss their clinical features.

Zenner [31] reported a case of sarcoma occupying the greater part of the left occipital lobe with complete right homonymous hemianopia up to the fixation point, slight variable weakness of the right arm and leg, difficulty in finding the right word and alexia.

Mills and others [20] mentioned the difficulty of differentiating a tumour of the occipital lobe from one of the cerebellum and quoted Weeks [29], who stated that papillœdema had been found in approximately 87 per cent. of both pre-occipital and cerebellar tumours in a series of 677 cases of cerebral tumour he had reviewed.

Knapp [17] examined the incidence of mental symptoms with cerebral tumours affecting different parts of the brain. Of four cases of occipital tumour mental symptoms had been present in three. He quoted Schuster [23] who had found 4·3 per cent. of occipital tumours among 775 collected cases of cerebral tumour, and mental symptoms in 60 per cent. of those affecting the occipital lobe.

Cushing and his co-workers [6] created renewed interest in the value of the examination of the visual fields in the localization of cerebral tumours, and in particular differentiated the quadrantic defects in the visual fields occurring with tumours deep in the temporal lobe.

Weisenburg [30] reported a case of tumour of the right occipital lobe, with pressure upon the sensory and motor fibres of the same side and extension into the occipital lobe of the other side. Jamieson [15] had previously reported a case of this type in a patient who was blind. the blindness being regarded as double hemianopia due to involvement of the optic radiations on both sides. In this case the tumour affected first the optic radiation on the left side and later that on the right side. In Weisenburg's case, however, the tumour affected the second optic radiation only partially and so produced a left homonymous hemianopia, together with a right homonymous quadrantic defect affecting only the upper quadrants. The patient also had irritative visual phenomena, at first seeing objects one above the other when they were not so and later seeing objects in the left visual fields jumbled up to look like scenery, glass or a lot of bricks.

Climenko [5] reported a case in which a tumour of the right occipital lobe was associated with a left homonymous quadrantic defect of the visual fields. The patient saw many-coloured animals and objects before his eyes when his headache became severe, and at times saw myriads of rapidly moving objects and various colours. Loud splitting noises like those of a hammer on an anvil were heard when the headache was severe. The left homonymous defect in the visual fields was characterized by blindness of the whole of the upper quadrant and of a small portion of the lower quadrant. In a series of 99 brain tumours recorded in 1916, Clarke [4] found four tumours of the occipital lobe, three of which were gliomata and one an endothelioma.

Bregman and Mesz [2] described a case of angioma of the left occipital region associated with a systolic bruit, marked apertures in the overlying bone on X-ray examination, paresis of the left arm and leg, nystagmus on looking to the left and a nævus of the scalp over the affected area. Puusepp [22] reviewed the clinical features of eight cases of tumour of the occipital lobe, in all of which headache, vomiting, motor and sensory symptoms, papillœdema and hemianopia were present.

Recently, Frazier and Waggoner [9] made the first critical survey of the clinical features of tumours of the occipital lobe in a paper given before the Philadelphia Neurological Society. These writers surveyed forty cases, in nine of which the tumour had invaded the occipital lobe from the adjacent part of the temporal lobe. They found convulsions in 25 per cent., papillœdema in 67·5 per cent., headache as an important symptom in 90 per cent., and inequality of the pupils with the larger pupil on the contralateral side in 25 per cent. In 7·5 per cent. no definite localizing signs were available, since the tumour involved the convex surface of the occipital lobe, a silent area. In some cases there was a reasonable doubt as to the side on which the tumour was situated apart from the symptoms of involvement of adjacent structures. Of these, signs indicating involvement of the parietal lobe—diminution of stereognostic perception, hemiparesis, hemianæsthesia, deviation of the tongue to one side, and lower facial weakness—were found to be most useful. Aphasia was present in approximately 12·5 per cent. when the tumour was adjacent to or involved the temporal lobe. Symptoms suggesting dysfunction of the frontal lobe, which occurred in a maximum of 10 per cent., were sometimes a source of confusion. Cerebellar symptoms were often conspicuous and were regarded as indicating the presence of a tumour in close relation to the tentorium cerebelli. A staggering gait and nystagmus were found most often in from 10 to 12 per cent., while ataxia, awkward movements of the hands, past-pointing and asynergia were found in only from 2 to 5 per cent. Waggoner regarded hemianopia as the most important sign in localization, and found that none of the cases bore out the conception that hemianopia of occipital origin was less clear-cut than that due to lesions further forward.

The position of the knowledge in regard to the clinical features of occipital tumours as revealed in the literature may therefore be summed up as follows: (1) Symptoms of increased intracranial pressure have been of most value in drawing attention to the condition, while visual hallucinations, both formed and unformed, have been recorded as occurring, though rather infrequently. (2) Distortions of the visual fields have been regarded as the most important evidence of localization except in those cases in which the convex surface of the occipital lobe has been affected. Though unusual types of field defects have been reported in individual cases, dogmatic statements persist in some quarters that homonymous hemianopia up to the fixation point and in others that homonymous hemianopia with spacing of the field for central vision are characteristic of tumours of the occipital lobe. Though complete hemianopia, hemianopia with preservation of the field for central vision, partial hemianopia, and quadrantic defects have all been described in reports of individual cases, little attention has been paid to the possibility of variations in the visual field defects with occipital tumours. (3) Neighbourhood symptoms and physical signs have recently been regarded as important in the lateral and differential localization of tumours of the occipital lobe.

III.—The Symptoms of Occipital Tumours.

As a rule the symptoms of a focal lesion of the brain may be discussed under the following heads: (1) the symptom or symptoms which first drew attention to the presence of an intracranial condition; (2) the symptoms directly attributable to involvement of the part affected; (3) those due to interference with the functions of adjacent structures; and (4) those which can be attributed to a general increase in intracranial pressure. In studying the symptoms of tumours of the occipital lobe it was soon evident, however, that such a dogmatic classification of symptoms *per se* was not at once possible, as the origin of many of them was more or less obscure. Further, while it seemed possible to arrive at the cause of many symptoms which were of a negative character the sense that they indicated a diminution or abolition of function, it was impossible to determine the source of those which were of a positive character and might have been due as much to release of the function of adjacent or associated parts, or to stimulation of the functions of the parts directly involved.

(1) *The first symptom.*—The symptoms which first drew attention to the presence of an intracranial lesion varied considerably. In approximately 75 per cent. of cases they appeared to be directly attributable to a general increase in intracranial pressure, while in the remaining 25 per cent. they were more or less of a focal nature.

In 30 per cent. of cases the onset of the condition was heralded by an epileptiform attack or by a sudden loss of consciousness, but in only one-third of these cases was the attack preceded by a visual aura. In only one case did visual hallucinations alone draw attention to the condition. In 35 per cent. headache of frontal, occipital or general distribution was the initial symptom. In 17 per cent. symptoms of general mental impairment, such as failure of memory, disorders of conduct, change in character or "neurasthenia," were present for a long time before the presence of an intracranial tumour was suspected. In 15 per cent. a transient loss or progressive failure of vision first drew attention to the condition. In one case a squint was noticed before any other symptom appeared. Aphasia was a prominent early symptom in at least three cases—"an inability to find the right word"—in two cases in association with epileptiform attacks, and in one case with failure of memory. Apart from the occurrence of a visual aura in 10 per cent. of cases and of visual hallucinations in one case, the initial symptom did not suggest that the occipital lobe might be affected. In fact, throughout, symptoms suggesting involvement of the occipital lobe were comparatively infrequent, and were confined to visual hallucinations and to symptoms suggesting that part of the visual field was blind.

(2) *Visual hallucinations.*—These occurred at some time in the clinical course in 25 per cent. of the cases studied, and in 15 per cent. were the typical "unformed" images of an occipital lesion. In only 10 per cent. of cases did the visual hallucinations represent the aura of an epileptiform attack.

"*Unformed*" *hallucinations* occurred in the following cases. (*a*) The patient saw white lights dancing straight in front of the eyes for ten minutes at a time. An endothelioma was found growing from the falx cerebri, invading the inner aspect of the occipital lobe and damaging the optic radiation anterior to the calcarine cortex. (*b*) For five years the patient, aged 12 years, had suffered from attacks of *petit mal* characterized by a sudden loss of consciousness and associated with a visual aura. Before the attack something seemed to come over the eyes, especially on the right side, and after a short time flashes of light appeared in front of the right eye. At operation a tumour was found deep in the left occipital lobe. (*c*) Twelve months before he was first seen the patient had a bilious attack during which he saw a round ball of bright light in front of the right eye. Since then he had been conscious of a black disc with a light behind it, always moving about in front of the right eye and preventing him seeing things. At operation, a tumour involving the left occipital lobe was exposed and patches were seen coming to the surface in the region of the left supramarginal gyrus. (*d*) The patient had had four major epileptic fits, two of which were preceded by an aura of "flashes of flame" before the eyes. The visual fields were normal. A hard, pearly tumour the size of a golf ball was removed from the outer surface of the right occipital lobe about two inches in front of the occipital pole. (*e*) Epileptic fits occurred six months before the patient was first seen and were preceded by a visual aura. "Flashes of light" were seen from time to time for fourteen days before the first fit. The visual fields were normal. An hydatid cyst was removed from the outer surface of the right occipital lobe behind the supramarginal gyrus. (*f*) Two years before he was first seen the patient suddenly saw a series of flashes which seemed to come from above downwards in the right visual field. The flashes were alternately blue and red, and seemed to be brilliant though dark. They continued rhythmically and regularly for about fifteen minutes and prevented the patient seeing anything else. They were described as being narrow lines like lightning, but straight. Subsequently these attacks occurred about twice a week for fifteen minutes at a time. At other times the patient was conscious of an object moving up and down to the right of the middle line. A gumma was found infiltrating the inner aspect of the left occipital pole over an area about three centimetres in diameter.

Distortion of visual images occurred in two cases. In the case last mentioned the patient remarked that the edge of the pavement on his right appeared to be converging towards the fence on his left. In a further case there seemed to be a mist with specks in front of the eyes, and at intervals "everything seemed to be long and tall." The visual fields were unaffected. A tumour about the size of a golf ball and firm in consistence was found coming to the surface over an area about two and a half centimetres in diameter on the outer aspect of the left occipital lobe near the pole.

A "formed" visual hallucination occurred in two cases. Auditory hallucinations which sometimes assumed the form of his teacher's voice speaking to the patient were associated with a visual hallucination in the form of the teacher himself. A large cystic glioma was found occupying the anterior part of the occipital lobe and the adjacent part of the temporal lobe. The "formed" hallucination in the second case is described in the paragraph on auditory hallucinations. Occurring in a patient with a tumour of the occipital and temporal lobes it took the form of an old woman with a hood coming towards the patient. It was associated with "formed" auditory hallucinations.

In a further case there was *difficulty in recognizing objects,* an abnormality which might be described more accurately as a failure of picture memory. In addition, however, the patient did not know through which window to look to see objects with which he had been acquainted for many years. As in this case the splenium of the corpus callosum was involved as well as the occipital lobe, it was possible that the interruption of the normal association paths between the two occipital lobes prevented the patient localizing objects satisfactorily.

It is interesting to note that in 75 per cent. of the cases of occipital tumour studied no visual hallucinations occurred at any stage of the clinical course.

In few of the cases without hallucinations the visual fields were entirely unaffected, though in some there was a mere constriction of the contralateral temporal and of the homolateral nasal field, and in many the field for central vision was unaffected. In those cases in which the tumour was confined to the occipital lobe at or near the pole the visual hallucinations, when present, were always of the "unformed" type, and occurred both in cases in which the visual fields were unaffected and in those in which hemianopia was present either up to the fixation point or with spacing of the field for central vision. Visual hallucinations would appear to have occurred, therefore, both when the physiological continuity of the visual fibres was unaffected and when it was completely interrupted. It is apparent that normal visual paths must have been present to convey stimuli from the level of the lesion to the areas of the cerebral cortex in which the stimuli were interpreted as flashes of light and colour; but that complete physiological continuity of the path from the periphery to the visuo-psychic area was not essential. It was equally apparent, however, that in most cases the physiological continuity of some or all of the visual fibres was unaffected, as was shown by preservation of the greater part of the visual field or of that for central vision only. Hence it might be concluded, as suggested by Harris [12], that in the presence of a lesion affecting the visual path, visual hallucinations are more likely to occur when the central visual apparatus is at the same time exposed to stimuli from the periphery. Stimulation of the visual fibres at the level of the lesion, and preservation of the physiological continuity of the visual path from the level of the lesion to the visuo-psychic area would appear to be the conditions essential for the occurrence of visual hallucinations, and to be more likely to produce them when at the same time the physiological continuity of the visual path from the periphery is more or less preserved. This explanation is the only one which takes account of the occurrence of visual hallucinations with hemianopia up to the fixation point.

Furthermore, the conditions under which visual hallucinations occur: (1) with normal visual fields but with a tumour adjacent to the visual fibres among which changes due to variations in circulation or to œdema are apt to occur; and (2) with a tumour situated at or near the occipital pole and producing complete or partial interruption of the visual path, suggest that comparatively few of the visual fibres may be affected and that the few stimuli arising from the affected fibres must of necessity be interpreted as simple and unformed objects.

The occurrence of formed and complex visual hallucinations in association with a tumour in the anterior part of the occipital lobe and encroaching on the posterior part of the temporal lobe would likewise appear to depend on the stimulation of numerous visual fibres and on the normal stimuli arising from the periphery. The more numerous and diverse stimuli arising from such a lesion are interpreted with less difficulty as an object with the mental picture of which the patient has had some previous acquaintance.

The occurrence of distortion of visual images in two cases, one in which the lesion probably involved the visuo-sensory area, and the other in which it involved the visuo-psychic area, is of particular significance. It would seem that partial interruption of the visual path at a higher level, whether at the visuo-sensory level or between that and the visuo-psychic level, while permitting a correct interpretation of the nature of the object, may at the same time lead to apparent distortions of shape, size and form. In addition, the actual failure of picture memory when the lesion is situated a little anterior to the visuo-psychic area and in the region of the left supramarginal gyrus, suggests that the latter is the result of a similar interruption of physiological continuity at a slightly higher level in the visuo-sensory system. Though suggestive, the evidence of one case is insufficient to show that defects in the localization of objects which have been seen repeatedly is the result of disturbance of the normal association between the two occipital lobes by a lesion of the splenium of the corpus callosum.

(3) *Symptoms suggesting abnormality of the visual fields.*—As a rule, when the visual fields are affected suddenly, the patient is aware of the defect at once. Such is usually the experience of patients in whom thrombosis of the occipital artery occurs on one or both sides. It was unusual, however, for the patient to be aware of the defect in those cases in which the visual fields were affected as the result of an occipital tumour. In only 16 per cent. could the patient recall an experience which indicated that his visual field was limited on one side. This experience varied in different patients. Usually the patient found himself colliding with people on the affected side and sometimes he collided with objects as he walked round them. In only one case did the patient state definitely that he could not see on the affected side. The patient, who was a golfer, gave a very suggestive history. He collided with objects on his left as he passed them. Also when he pulled a ball at golf it at once disappeared from view, but when he sliced it remained in view for the greater part of its flight. In many cases an obscuring of perception, as a result of increased intracranial pressure, may have explained why the patient was unaware of his defect. In

others it was probable that the defect developed so gradually that he readily adapted himself to it.

The above symptoms represent those which may be fairly attributed to involvement of the occipital lobe. It is obvious that by extension, or by œdema or vascular changes adjacent to it, a tumour of the occipital lobe may result in symptoms which suggest involvement of the temporal or parietal lobes, of the speech centres or of the cerebellum. In addition, the general increase in intracranial pressure resulting from the presence of the tumour may also produce symptoms and physical signs which suggest involvement of structures at some distance from the original lesion. These two groups of symptoms are considered below.

(4) *Epileptiform attacks or loss of consciousness.*—Epileptiform attacks or sudden loss of consciousness occurred in 52·5 per cent. of the cases studied, and in 30 per cent. were the symptoms which first drew attention to the presence of an intracranial lesion. In only 10 per cent., however, were the attacks preceded by a visual aura. Epileptic attacks, therefore, occurred much more frequently in this series of tumours of the occipital lobe than in an average series of tumours of the brain.

In order to find if there was any direct relationship between the position of the tumour and the incidence of epileptiform attacks, those cases in which they occurred were classified according to the parts involved. Of the twenty-four cases in which the tumour was confined to the occipital lobe, epileptic attacks occurred in only 8 cases; while of the ten cases in which the temporal lobe was involved as well attacks occurred in five cases; and of the six cases in which the parietal lobe was involved as well attacks occurred in five cases. These figures suggested that epileptic attacks were probably less frequent in those cases in which the tumour was confined to the occipital lobe, and relatively more frequent if the temporal or parietal lobe was involved as well.

The relationship of the occurrence of epileptic attacks to the presence of increased intracranial pressure at the time they occurred demands some consideration. Accepting headache, vomiting, vertigo and papillœdema as a fair indication of the presence of increased intracranial pressure, it was found that in very few cases were the attacks related to the presence of increased intracranial pressure which had become definitely established. More often, however, they were related to sudden crises of headache, vomiting and vertigo which were presumably manifestations of a temporary increase in intracranial tension. In such cases the attacks were often followed by weakness of one or more limbs, which either persisted or recovered in a few days. Occasionally an epileptiform attack of a "focal" type occurred, but that was the exception.

It was unusual for the attacks to be numerous. In only two cases did the clinical picture assume the characteristics of "idiopathic epilepsy," in one case for two years and in the other for five years, before other symptoms and physical signs appeared. More often other symptoms appeared within a few weeks and left no doubt that the attacks had an organic basis. As a rule, apart from the two cases mentioned, the patient had from one to six attacks before coming under observation.

In spite of the apparent influence of the focal lesion, œdema, vascular changes and temporary or permanently increased intracranial pressure upon the occurrence of epileptiform attacks, it was evident that some factor other than focal irritation or increased intracranial tension must have played a part in many cases. It many cases in which the lesion was equally of a focal type or the intracranial pressure was raised no such attacks occurred.

The details of the attacks themselves were difficult to determine, as in most cases it was necessary to depend upon relatives for a description. Often, however, it was possible to obtain sufficient information upon which to identify the nature of the attacks. They were of the following types: (*a*) sudden loss of consciousness and a fall without any convulsions; (*b*) epileptiform attacks of a Jacksonian type; (*c*) major epileptiform attacks with general convulsions; and (*d*) attacks of *petit mal* with or without a visual aura.

Occasionally the attacks were preceded by an aura—visual, auditory or sensory, and sometimes a feeling of cramp in one limb. The occurrence of a visual aura usually indicated that some part of the visual path was involved, probably in the occipital lobe, but did not suggest that the tumour itself had involved the visual fibres. The occurrence of a "formed" visual hallucination before a fit suggested involvement of the anterior part of the occipital lobe or extension into the temporal lobe. Unformed auditory or sensory hallucinations, such as noises in the ear, numbness or tingling, occurred sometimes when the temporal or parietal lobes were invaded, but more often when the tumour was confined to the occipital lobe. They were thus of no value in detailed localization. Formed auditory hallucinations, however, taking the form of voices speaking and in some cases conveying definite information, occurred only when the anterior part of the occipital lobe and the adjacent part of the temporal lobe were involved. Unformed auditory and sensory aura, local cramps in one limb, and both transient and permanent weakness of an arm and a leg after an attack, occurred in cases in which the tumour was entirely confined to the occipital lobe, and did not necessarily indicate that the tumour had invaded the temporal or the parietal lobe.

(5) *Auditory hallucinations.*—Noises were heard by the patient, usually before a fit, in two cases. In one case they preceded the onset of symptoms suggesting a transient increase in intracranial pressure. Sometimes they were like the buzzing of bees or of voices, but often they formed themselves into the voice of the patient's teacher speaking to him. The teacher's words seemed to be a repetition of something the patient had heard him say, but the actual words were never heard. A formed visual hallucination of the figure of the teacher was sometimes associated with the auditory hallucination. The tumour was found to involve the anterior part of the occipital lobe and the posterior part of the temporal lobe.

In the second case the auditory and visual hallucinations were described by the patient as follows : " When I have the heavy feeling coming over me, I see gold stars falling in front of me. They are in front and not to one side. Then I see sort of wings flapping. Also I hear a sort of 'ha-ha'ing in the ears ; and sometimes a voice, a strange voice like nothing earthly, saying, ' Why have you not told me before? Why did you not tell me long ago ?' Sometimes I see an old woman with a hood coming towards me. Then I feel a strange heavy sinking sensation in the pit of the stomach. Then I lose myself." In this case the tumour was found occupying the adjacent parts of the occipital and temporal lobes.

(6) *Headache.*—Headache was present in 95 per cent. of the cases studied and in 35 per cent. was the first symptom. In practically every case it was associated with other symptoms and physical findings indicative of increased intracranial pressure. In two cases, however, it was absent, though a moderate degree of papillœdema was present in each case. No characteristic distribution of the headache was noted. While usually frontal or vertical in distribution, it sometimes involved the occipital region as well. Occurring at first at infrequent intervals, usually on arising in the morning and improving later in the day, it became gradually more frequent and severe, and was associated with nausea, vomiting and giddiness. Finally, in some cases it awakened the patient during the night and persisted for as long as five days at a time.

Acute crises of increased intracranial pressure characterized by severe headache, vomiting and vertigo, sometimes occurred at long intervals before the headache became permanent. Rarely, an attack of headache occurred in which the distribution was entirely occipital. As was to be expected, however, when the headache was almost always associated with increased intracranial pressure, its distribution gave no clue whatever to the site of the lesion.

(7) *Vomiting.*—Vomiting was usually absent in the early stages of a case of occipital tumour, even when severe morning headaches occurred. However, on the headache becoming more severe and prolonged, it was usually associated with nausea. Eventually vomiting occurred during such attacks. It occurred often at the height of the headache, sometimes once on getting out of bed and sometimes only once or twice during the whole course of the illness. In about 20 per cent. of cases vomiting did not occur, though a moderate or severe degree of papillœdema was present.

(8) *Vertigo.*—Vertigo was an infrequent symptom even during the crises of increased intracranial pressure characterized by severe attacks of headache and sometimes by vomiting. " A swimming in the head " was more usual. The feeling that objects were moving round was not experienced, nor was a sensation of falling in one particular direction. Occasionally the patient tended to go to one side or the other, a tendency which was satisfactorily explained by disturbances of motor function on one side of the body.

(9) *Diplopia.*—Diplopia, occurring either intermittently or for a month or two at a time, was not common. It occurred in only 22 per cent. of the cases studied. The duplication of images usually occurred on lateral deviation of the eyeballs, was associated with a slight defect of lateral deviation to one or both sides, and sometimes with slight irregular nystagmoid jerkings of the eyeballs on lateral deviation. When present diplopia was invariably associated with an increase in intracranial pressure. In at least nine cases in which there was a definite increase in pressure no history of diplopia was elicited.

(10) *Impairment of vision.*—Impairment of vision appeared as a definite symptom in 57 per cent. of cases and was the initial symptom in 15 per cent. Occasionally the failure of vision was intermittent, objects being dark before one or both eyes for a day or two at a time. Such intermittent impairment of vision was particularly apt to occur during the crises of increased intracranial pressure. It was a common statement of the patient that objects looked at appeared to be dim for

an hour or two after an attack of headache. In one case dimness of vision and what was practically blindness appeared after seeing a series of bright lights. In other cases difficulty in seeing letters and words was noticed early in the history of the condition, the difficulty becoming more pronounced as the condition progressed. More often the patient complained of a mist with specks in front of the eyes. These variations in vision were almost invariably associated with papilloedema, and sometimes when progressive with the development of secondary atrophic changes in the optic disc.

(11) *Abnormal tastes and smells.*—The patient complained of abnormal tastes and smells either alone or before a fit in five cases, in three of which the tumour was confined to the occipital lobe, and in two of which the tumour involved the temporal lobe as well. In no case could the taste and smell be identified, though in two cases a resemblance was noticed between the taste or smell and that of something of which the patient had had previous experience. One patient in whom there was a tumour towards the external surface of the left occipital and temporal lobes was for two months conscious of a peculiar smell which he failed to identify. Another patient occasionally had a taste like blood in the mouth, and here again the tumour involved the left occipital and part of the left temporal lobe. In the remaining three cases in which the tumour was confined to the occipital lobe the smell or taste was described as unpleasant but could not be recognized.

(12) *Disturbances of the speech functions.*—A history of disturbance of the speech functions was particularly valuable in the localization of a tumour affecting or spreading to the outer surface of the left occipital lobe. The speech functions were affected in 35 per cent. of the cases studied. When the parietal lobe was affected in addition to the occipital lobe, or the tumour extended to the outer surface of the occipital lobe, the speech defect was more or less permanent. A transient attack of motor aphasia or difficulty in finding the right word was common for a short time after an epileptiform attack.

The commonest defect was failure of picture memory, either of individuals, objects, words or letters; and frequently one function alone was affected. In 25 per cent. there was alexia or failure of picture memory. In four of these cases there was also difficulty in finding the right word, and in several others in which the left occipital lobe was involved there was transient difficulty in finding the right word during acute crises of increased intracranial pressure. As a rule the patient complained that he could not read words or letters, but one patient, a cartoonist, was known to have been making his figures without arms or legs. The details of the disturbances of speech functions and their relation to the pathological changes present are dealt with in the discussion of the physical signs.

(13) *Subjective sensations.*—Spontaneous subjective sensations were present in 30 per cent. of cases; were associated with involvement of the occipital lobe alone in 10 per cent.; of the occipital and temporal lobe as well in 10 per cent.; and of the occipital and the parietal lobe as well in 10 per cent. The subjective sensations occurring with tumours of the occipital lobe alone were a feeling of numbness, coldness or tingling in the contralateral arm or leg. In one case there were spasmodic attacks of pain in the right side of the face, which probably had no direct relation to the tumour itself. In one case in which the tumour extended into the temporal lobe there was a constant feeling of cold and shivering all over the body.

(14) *Disturbances of motor functions.*—In some cases the nature of the disturbances of motor function as described in the history suggested lesions of motor fibres, and in others disturbances of cerebellar function. They were present in 52 per cent. of the cases studied.

In 40 per cent. of the cases the symptoms suggested involvement of the motor fibres. In some they appeared suddenly after an epileptiform attack, and in others they came on gradually in the later stages of the illness. One patient in whom the tumour had extended slightly into the left parietal lobe had noticed that the right leg was dragging for three weeks. In a second patient the left arm and leg became weak after two epileptiform attacks two months before admission. She complained that she dropped things from the left hand and dragged the left foot when walking. In a third patient similar symptoms appeared after an epileptiform attack, and in a fourth patient they developed gradually. In these cases the symptoms suggesting involvement of the motor fibres were comparatively indefinite. In no case did the frank symptoms of a hemiplegia appear.

In 18 per cent. of cases the tumour had extended into the adjacent parietal lobe but never far enough to damage the motor fibres by direct involvement. In about half of these cases spontaneous subjective sensations were present as well as weakness of the contralateral limbs. In the remaining 22 per cent. the tumour was confined to the occipital lobe and in about three-quarters of these cases spontaneous subjective sensations occurred in addition to the motor weakness.

In 12 per cent. of cases the history of motor weakness suggested disturbance of the cerebellar functions. Symptoms of this type were a tendency to fall backwards or to one side, weakness of the arm and leg often on the same side as the tumour, and difficulty in controlling the movements of the limbs.

(15) *Disturbances of the sphincters.*—Difficulty in controlling the sphincters was not a characteristic feature of occipital tumours *per se.* Incontinence of urine and fæces occurred at some stages of the clinical course in 12 per cent. of cases. As a rule, it was present during acute crises of increased intracranial pressure and disappeared as soon as the patient recovered from them. In one case it appeared during the late stages of the illness but disappeared when the intracranial pressure was relieved by surgical measures. Incontinence occurred, however, in only a few of the cases in which the intracranial pressure was much raised. In spite of this the evidence would appear to show that rapid increase in the intracranial pressure was the important factor in the production of incontinence, and that the situation of the tumour and other changes in the brain bore no relation to it.

(16) *Mental symptoms.*—Mental symptoms of varying severity appeared in 55 per cent. of the cases studied, and in 17 per cent. were the clinical features which first drew attention to the illness.

As the latter were often of considerable importance in differential diagnosis they are described in detail. In Case 3 the patient's memory for recent events was affected first, but this was soon followed by difficulty in reading and inability to find the right word. In Case 7 the patient felt for a long time that he was getting run down, he was tremulous and had no confidence in himself. In Case 10 the patient was easily excited, lost his temper too easily, and found that his memory for recent events was failing rapidly. In Case 16 the patient had been thought for many months to be suffering from neurasthenia. In Case 32 the patient noticed a general failure of health and felt that he wanted to get away from everything. He often forgot where he was going. In Case 25 the patient had suffered from neurasthenia for sixteen months and was sure that his brain was going. In Case 37 the patient had felt tired for five years, and for three years had shown a definite change in character.

Most of the mental symptoms which occurred in the early stages of the illness were of the psycho-neurotic type as if the patient were less able to adapt himself to his environment and to meet his difficulties. For a time they appeared to justify a diagnosis of neurasthenia.

The mental symptoms occurring during and after the onset of acute crises of increased intracranial pressure varied considerably. In the simpler cases the patient was merely drowsy and confused. In more pronounced cases he became comatose for a time, and on recovering was confused for an appreciable period. During a crisis one patient was incoherent in speech and failed to recognize his relatives. Another patient was drowsy during the attacks of headache and became more drowsy with successive attacks. In all such cases the mental symptoms were intermittent, the patient returning to a more or less normal degree of mental health between the attacks.

In the more slowly progressive cases the mental symptoms were as follows: Impairment of recent memory, absent-mindedness, excitability, irritability, lack of confidence, inability to think clearly, feeling weak and tired, restlessness, suspicion and making peculiar remarks. These symptoms were of considerable importance. They often occurred before the onset of frank symptoms of increased intracranial pressure when their appearance might easily have led to the suspicion that the tumour had originated in the frontal lobe. Even when they occurred after symptoms of increased intracranial pressure had appeared, they might have been regarded as of the same significance.

IV.—The Physical Signs of Occipital Tumours.

It is most convenient to discuss the physical signs found in association with tumours of the occipital lobe in the order in which they are elicited during the routine examination of the patient. The term "physical sign" is used here to include all evidences of abnormality elicited during the examination of the patient.

(1) *Mental changes*—These were found on examination in 60 per cent. of the cases studied. In every case they were associated with increased intracranial pressure at the time the examination was made. There were, however, several cases with increased intracranial pressure in which no definite psychological abnormalities were found. Some degree of mental impairment was present in all the above 60 per cent., if the ability of the patient to meet the situations of his everyday life were taken as the standard of normality.

The commonest defects were defects of attention and memory, comparatively slight and appearing only under the influence of stress or fatigue in the slighter cases, but very pronounced and constant in the severe cases. In 17 per cent. the patient was unable to fix his attention for any appreciable time; in 7 per cent. he failed to co-operate satisfactorily during examination; and in 12 per cent. cerebration was definitely slow. In at least 22 per cent. there was definite clouding of consciousness with drowsiness and lethargy. Insight was definitely impaired in one case only.

Attention was impaired in more than half the cases in that the patient had to have his attention repeatedly drawn to a statement or a command; while in two cases the patient had to be roused from his lethargic condition and spoken to repeatedly before he could appreciate what was expected of him.

Orientation was normal in most cases, but in 10 per cent. there was definite disorientation both as to time and place. In one other case the patient was correctly orientated as to time and place but failed to decide whether he was to the left or right of a fireplace near him. In a further case the patient was unable to find his way about in places he knew well, and did not know through which window to look to see objects he had known for many years. As suggested above, these apparent disorders of orientation probably have a more local significance than the disorientation as to time and place which occurs with mental impairment.

Memory was affected in 32 per cent. of cases. As a rule the patient was unable to remember the details of incidents which had occurred a few minutes before; but in 12 per cent. with definite impairment of cerebration there was also mental confusion and loss of memory for remote events. At the same time, the time relations of both recent and remote events were much confused.

Reasoning power was definitely impaired in two cases and speech was incoherent or irrelevant apart from aphasia in three cases. As a rule the patient was emotionally colourless and detached, occasionally he was worried about his condition and his difficulties with speech, while in one case he was definitely facile and euphoric.

Hallucinations and illusions which could be ascribed to mental changes rather than to interference by organic conditions with visual, auditory and sensory paths were practically unknown. One patient, however, regarded his doctor as a policeman, while another became exceedingly suspicious and antagonistic towards those with whom he had been on good terms. In only one case did the hallucination based upon the organic lesions lead to the development of delusions.

(2) *Variations in the sense of smell.*—In 12 per cent. of cases there was difficulty in recognizing the smell of test substances such as cloves, peppermint, lavender and paraldehyde. In one case the presence of nasal catarrh was enough to account for the impairment of smell; while

in three others the mental condition was much impaired at the time the patient was examined. In these three cases the patient was unable to recognize such test substances as cloves and peppermint, but knew that lavender and paraldehyde were different. It was apparent that minor differences were not recognized, whereas definite distinctions were appreciated though not by name. In a further case the sense of smell was completely lost in the left nostril but normal in the right nostril.

(3) *Variations in the visual fields.*—Detailed charts of the visual fields were available in 80 per cent. of the cases studied. In the remaining 20 per cent. it was found impossible to chart the fields because the patient was mentally impaired or was unable to co-operate well enough during the examination. In these cases, however, it was often possible to determine roughly the type of defect in the visual fields.

The following conclusions are based only on those cases in which a detailed record of the visual fields was available, though the percentages given are calculated from the total number of cases studied. In every case but two there was some degree of homonymous hemianopia on the side opposite to that on which the tumour was situated. In individual cases, however, the defect in the visual fields varied considerably with the position of the tumour.

Classified according to the type of the defect in the visual fields, the cases studied were grouped as follows:—

(*a*) Those with complete contralateral homonymous hemianopia extending right up to the fixation point (32·5 per cent.).

(*b*) Those with incomplete contralateral homonymous hemianopia extending to the middle line above and below the field for central vision but leaving the latter more or less unaffected (22·5 per cent.).

(*c*) Those in which there was a contralateral homonymous crescentic defect of the visual fields (7·5 per cent.).

(*d*) Those in which there was a contralateral homonymous quadrantic defect of the visual fields (12·5 per cent.)

(*e*) Those in which the visual fields were normal (5 per cent.).

In addition, there was often superimposed on these types of fields a certain degree of concentric constriction in those cases in which papillœdema had been present for some time or in which optic atrophy was beginning.

(*a*) *Contralateral homonymous hemianopia up to the fixation point.*—This type of defect in the visual fields was found in 32·5 per cent. of cases; and in 5 per cent. of cases unformed visual hallucinations had occurred before and up to the time the visual field defect was discovered.

The temporal and nasal fields were definitely separated by a line which passed directly through the fixation point. The affected temporal and nasal fields were completely blind, while the corresponding nasal and temporal fields were either normal or showed a degree of peripheral constriction which depended upon the condition of the optic discs and the visual acuity.

The only points of importance in the pathological findings were that the position of the tumour was usually such that all of the visual fibres would have been involved by it, and that the proportion of cases in which degenerative changes had occurred was unusually high. Complete interruption of all the visual fibres was essential for the production of this type of field defect.

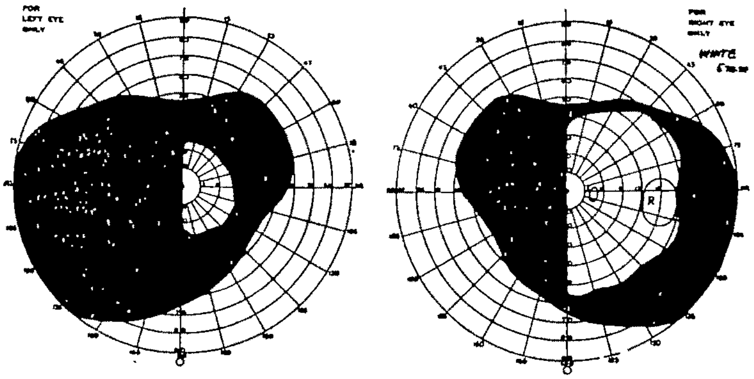

FIG. 1.—Contralateral homonymous hemianopia up to the fixation point due to an endothelioma weighing 135 grammes invading the right occipital lobe. (Case 10.)

(*b*) *Incomplete contralateral homonymous hemianopia with spacing of the field for central vision.*—This type of field defect occurred in 22·5 per cent. of cases and in only one case was associated with a history of unformed visual hallucinations. Above and below the field for central vision the nasal and temporal fields were more or less definitely separated by a vertical line through the fixation point of the normal field, though in some cases the dividing line extended a little towards the blind side. In all cases the field for central vision was more or less unaffected. In some there was definite and regular spacing at ten degrees from the fixation point, but in most cases the field for central vision was not so regularly and completely defined as it was in those cases in which thrombosis of the posterior cerebral artery had occurred in a comparatively young individual. In most cases the spacing of the field for central vision was irregular and varied from 5 to 10 degrees from the fixation point. In the majority of these cases the tumour extended chiefly towards the external surface of the occipital lobe, while in one case it occupied a position almost entirely internal to the ventricle.

(c) *Contralateral homonymous crescentic defect of the visual fields.*—This type of field defect occurred in 7·5 per cent. of cases. The homolateral halves of the visual fields were normal or only slightly reduced as a part of the general constriction of the visual fields associated with long-standing papillœdema or commencing optic atrophy. The contralateral halves of the visual fields were limited only on the corresponding side of a line drawn vertically through the fixation point. Beginning at the vertical line mentioned, the periphery of the field for peripheral vision was gradually reduced more and more as far as the horizontal limit of the upper quadrant, and then less and less until it again became normal at the vertical limit of the lower quadrant. In the affected temporal field the defect assumed the form of a broad crescent, extending from the periphery inwards, while in the affected nasal field it assumed the form of a narrower crescent at the periphery. Measured horizontally from the fixation point towards the periphery, the proportion of the temporal field affected was approximately the same as that of the nasal field affected as long as the vision and the condition of the fundi were the same in the two eyes.

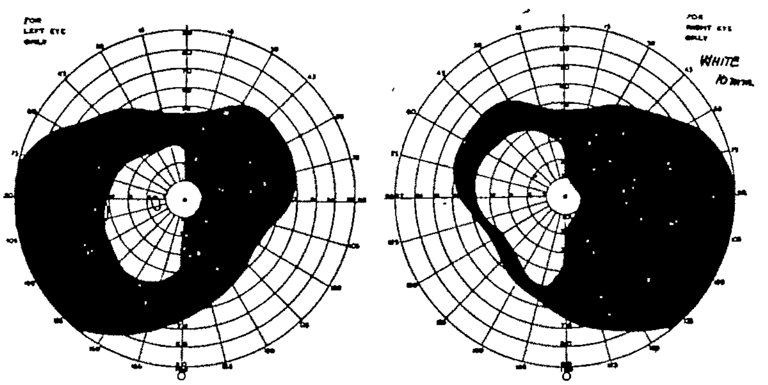

FIG. 2.—Contralateral homonymous hemianopia with sparing of the field for central vision, due to a tumour invading the mesial aspect of the left occipital lobe. (Case 20.)

The cases in which this type of field defect occurred appeared to have had in common the fact that the tumour in each case approached the optic radiation from the external surface of the occipital lobe.

Though there was insufficient evidence upon which to base any general conclusion, the association of a tumour in that position with a crescentic field defect was worthy of note.

(*d*) *Homonymous quadrantic defect of the visual fields.*—This type of defect of the visual fields occurred in 12·5 per cent. of cases. One quadrant of the contralateral temporal and the corresponding quadrant of the homolateral nasal field were completely blind at the periphery and the defect extended for a varying distance towards the fixation point.

A quadrantic field defect was present in two cases in which the tumour was situated in the anterior part of the occipital lobe and encroached upon the adjacent part of the temporal lobe; in two cases when the occipital lobe alone was affected, and in one case when part of the visuo-sensory area was probably affected. The following are summaries of the pathological conditions present, together with a description of the particular type of field defect found in each case.

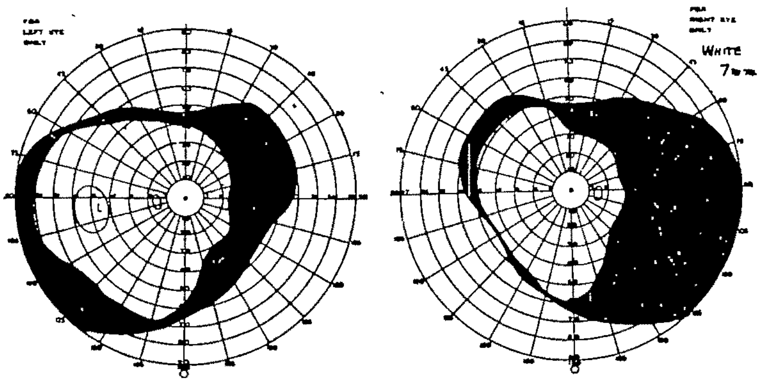

FIG. 3.—Contralateral homonymous crescentic defect of the visual fields due to a tumour invading the convex surface of the left occipital lobe. (Case 14.)

(i) A large glioma was found lying close beneath the cortex and occupying the whole of the posterior part of the left temporal lobe and the anterior part of the left occipital lobe. The lower right temporal quadrant showed a visual defect extending to within 30 degrees of the fixation point, while in the left lower nasal quadrant the defect extended right up to the fixation point. (Case 1.)

(ii) An endothelioma growing from the falx cerebri invaded the internal surface of the left occipital lobe about midway between its superior and inferior limits. Antero-posteriorly its position corresponded to a point about midway between the occipital pole and the posterior limb of the

Sylvian fissure. The right upper temporal quadrant showed a defect extending to within five degrees of the fixation point, while the left upper nasal quadrant showed a similar defect extending somewhat nearer to the fixation point. The greater part of the field for central vision was spared on each side. After the tumour was removed there developed a right homonymous hemianopia in which the greater part of the field for central vision was spared. (Case 12.)

(iii) A gumma invaded the inner aspect of the left occipital pole of over an area about three centimetres in diameter. There was general constriction of the visual fields and both the right lower temporal quadrant and the left lower nasal quadrant showed a defect limited to about the lower half of the quadrant and approaching to within five degrees of the fixation point. (Case 40.)

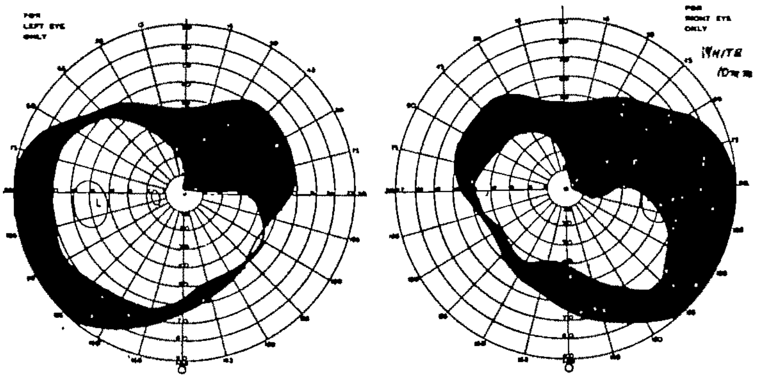

FIG 4.—Contralateral homonymous quadrantic defect of the visual fields due to an endothelioma invading the mesial aspect of the left occipital lobe just anterior to the calcarine cortex. (Case 12.)

In each of these cases it was apparent that the tumour affected only a portion of the visual fibres or, as in the last case, of the visuo-sensory cortex. In two of the cases the tumour was situated well forward in the occipital lobe, when it might be expected that the defects in the visual fields would be similar to those usually found with tumours of the temporal lobe. Persistent homonymous quadrantic defects of the visual fields are encountered frequently even in the later stages of tumours of the temporal lobe, but are found less often with tumours of the occipital lobe. It is possible, however, that if patients suffering from a tumour of the occipital lobe were studied carefully from the early stage of the illness quadrantic defects of the visual fields would be found more often. Nevertheless, it is important to note that quadrantic defects of the visual fields can and do occur when only a portion of the visual fibres are invaded by the tumour or even when a tumour invades only a part of the visuo-sensory cortex in the neighbourhood of the calcarine fissure.

(e) *Normal visual fields.*—The visual fields were found to be normal in 5 per cent. of cases. In each case the tumour involved the external surface of the occipital lobe. The following are the pathological findings in two cases of this type.

(i) From the outer surface of the right occipital lobe less than two inches in front of the occipital pole a hard pearly tumour about the size of a golf ball was removed. On section the tumour was found to be a gumma. A further examination of the patient four months after the operation showed that the visual fields were still normal. (Case 36.)

(ii) A cyst was removed from the outer surface of the right occipital lobe just behind the supra-marginal gyrus. Microscopical examination showed that the cyst contained a scolex with the characteristic features of *Tænia echinococcus.* (Case 38.)

In both of these cases the tumour was small, was confined to the outer surface of the right occipital lobe and apparently was associated with few changes in the neighbouring brain tissue. In each case it was only the history of a visual aura which made localization and treatment possible.

(4) *Changes in the fundi.*—In 65 per cent. of the cases studied, papillœdema was present, and in 45 per cent. the degree of swelling was over three dioptres. In 20 per cent. the discs were normal, in a further 10 per cent. they were doubtful but probably normal, while in the remaining 5 per cent. atrophic changes had already supervened. In Frazier and Waggoner's series of cases of occipital tumour papillœdema was present in 67·5 per cent., and in the majority of cases there were between three and five dioptres of swelling.

Frequently vision was normal, or only a little diminished, even in the presence of a high degree of papillœdema. When, however, the intracranial pressure had been increased for some time vision was definitely impaired, even in the absence of definite local evidence of atrophy of the optic discs. When atrophic changes were already present in the disc vision was often reduced to the perception of fingers only.

Retinal hæmorrhages were present only with the higher degrees of papillœdema. Occasionally, when the swelling of the discs was pronounced the development of a macular fan was observed. No evidence whatever was found to support the suggestion that retinal hæmorrhages were particularly apt to occur when the increase in intracranial pressure was the result of a tumour of the occipital lobe. The degree of pressure and the obstruction of retinal veins in their course behind the retina appeared to be the important factors in the incidence of retinal hæmorrhages.

(5) *The pupils.*—In the majority of cases the pupils were equal and reacted normally, whether the light stimulus were applied to the normal or to the blind side of the visual field. Occasionally they were dilated and reacted sluggishly, findings usually associated with some impairment of vision. Occasionally one or both pupils were slightly irregular in outline or eccentric, but nothing was found to account for these variations.

In 35 per cent. of cases the pupils were unequal, and in 25 per cent. the larger pupil was on the same side as the hemianopia or other visual field defect. In the remaining 10 per cent. the smaller pupil was on the same side as the visual field defect. Frazier and Waggoner found the pupils unequal, with the larger pupil on the contralateral side, in 22·5 per cent. of their cases. In no case in either series was the difference in the size of the pupils extreme.

Study of the vision in relation to this inequality of the pupils showed that there was no variation which could account for the contralateral pupil being the larger.

The fact that in 22·5 per cent. of Frazier and Waggoner's cases and in 25 per cent. of this series the contralateral pupil was the larger, suggested that there might be some direct relationship between the nature of the inequality of the pupils and the side on which the tumour was situated. However, the incidence of 10 per cent. of cases in this series in which the homolateral pupil was the larger had to be explained. No local conditions such as unilateral failure of vision or atrophy of the optic disc were found to account for the dilatation of the homolateral pupil. Consequently, it was impossible to arrive at any general conclusion other than that in two-thirds of the cases in which the pupils were unequal the larger pupil was on the contralateral side in relation to the position of the tumour, or on the same side as the visual field defect.

(6) *Ocular pareses and diplopia.*—Disturbances of ocular movements occurred in 30 per cent. of cases.

Most of the changes were those associated with paresis of the abducent nerve on one or both sides. As a rule the disturbances were slight and revealed themselves as a difficulty in deviating the eyeballs to one side or the other, or in irregular nystagmoid jerkings of the eyeballs on attempts at lateral deviation towards the affected side. During acute crises of increased intracranial tension, or late in the course of the case when intracranial tension was increased, definite internal strabismus was apparent. As a rule, the patient complained of diplopia, especially on lateral deviation during the acute phase, but did not do so during the chronic phase. These changes occurred in 17·5 per cent. of the cases. Since they were most pronounced during acute crises of increased pressure or in the long-standing cases in which the intracranial pressure was raised, it is probable that they were the direct result of the increased pressure upon the long and exposed course of the sixth nerve on each side.

In two cases some degree of bilateral ptosis was evident. In one case, though papillœdema was slight, the patient was drowsy and muddled and was constantly making an attempt to break through the fogged state in which he found himself (Case 13). In the second case there was a high degree of papillœdema and probably hydrocephalus.

In Case 18 there was difficulty in closing one eye on account of weakness of that side of the face ; in Case 26 there was proptosis of the left eye ; and in Case 27 there was a divergent strabismus of the left eye.

(7) *Nystagmus and nystagmoid jerkings.*—Jerking movements on lateral deviation of the eyeballs were found in 35 per cent. of the cases studied. These movements were of two distinct types : (*a*) nystagmoid jerkings ; and (*b*) a varying degree of true nystagmus.

(*a*) Nystagmoid jerkings occurred in 15 per cent. Fine horizontal movements, often irregular both in time and amplitude, occurred on lateral deviation of the eyeballs. Though sometimes present on lateral deviation to one side and not to the other, or more pronounced to one side and not to the other, they bore the same general characteristics throughout. They were associated in each case with a high degree of papillœdema and therefore with a pronounced increase of intracranial pressure. They were probably due to the difficulty of maintaining the lateral position of the eyeballs owing to lack of balance of the ocular muscles following pressure on one or both of the abducent nerves. The group of cases in which they occurred did not necessarily coincide with that in which the patient complained of diplopia or in which an internal strabismus was evident on lateral deviation. In no sense could these nystagmoid jerkings be ascribed to direct or indirect interference with cerebellar function.

(*b*) Movements which were very suggestive of true nystagmus occurred in 20 per cent. of cases. Because of the frequently quoted difficulty, in the absence of charts of the visual fields, of differentiating a tumour of the occipital lobe from one of the lateral lobe of the cerebellum on the same side, it was necessary to consider these cases in detail.

(i) In Case 8 there was rhythmic, horizontal and slow nystagmus on looking to the extreme right, and similar movements but of smaller amplitude on looking to the left. Associated features of the case were a high degree of papillœdema, definite paresis of the abducent nerve on each side and general muscular hypotonia more pronounced on the left than on the right side, though on the latter the tone was increased somewhat by a lesion of the motor fibres. A large perivascular sarcoma was found occupying the greater part of the left occipital lobe.

(ii) In Case 9 lateral deviation of the eyeballs to the left was accompanied by rhythmical horizontal nystagmus and that to the right by less marked nystagmoid jerks. Both discs were normal. The tumour involved the right occipital lobe.

(iii) In Case 10, on lateral deviation of the eyeballs to the right there were nystagmoid jerks of wide amplitude, while to the left there were a few fine jerks. In walking the patient showed a constant tendency to stagger to the right. A large endothelioma weighing 135 grm. occupied the right occipital lobe.

(iv) In Case 21 there was slight, horizontal nystagmus on looking to the right and the left—rapid, fine, irregular and ill-sustained. There was general hypotonia, especially on the right side, and inco-ordination with the finger-nose test, especially in the right hand. There was an extreme degree of papillœdema. The tumour occupied the left occipital lobe.

(v) In Case 23 there was regular nystagmus on looking to the left. A moderate degree of papillœdema was present. An ill-defined soft tumour was found about 1 in. below the outer surface of the right occipital lobe.

(vi) In Case 28 there was well-marked nystagmus at the rate of about five jerks per second on looking to the right. There were five dioptres of papillœdema in each eye. The tumour involved the left occipital lobe.

(vii) In Case 33 slow nystagmus was present with coarse movements on looking both to the right and to the left. A large thin-walled cyst occupied the right occipital lobe.

It was evident that in some cases the presence of nystagmus could be explained by cerebellar dysfunction secondary to increased intracranial pressure, the nystagmus and hypotonia being false localizing signs due to transmission of the high supratentorial pressure on to the cerebellum. In some cases direct local pressure on the cerebellum with or without increased intracranial pressure was responsible; in others a contrecoup pressure upon the contralateral lobe of the cerebellum may have occurred; while in others again no satisfactory explanation could be found to account for the presence of nystagmus. Distortion of the brain-stem owing to increased general pressure in addition to the lateral pressure may have accounted for some of the more obscure examples.

The following conclusions appeared to be justified on the evidence available in this series.

(*a*) Movements of the eyeballs resembling true nystagmus were present in 35 per cent. of the cases of tumour of the occipital lobe.

(*b*) In 15 per cent. of cases there was a mild degree of abducent paralysis on one or both sides which, on extreme lateral deviation of the eyeballs and the attempt to maintain the lateral position of the eyeball, resulted in nystagmoid jerkings.

(*c*) In 20 per cent. of cases there was nystagmus which suggested the presence of a cerebellar lesion—horizontal, slow and of full amplitude on lateral deviation to one side, and fast and of smaller amplitude on lateral deviation to the other side. In most of these cases the signs appeared after the onset of symptoms of increased intracranial pressure, and were the result of cerebellar dysfunction secondary to that condition. In the minority of these cases nystagmus was present throughout the clinical course and was associated with other symptoms which suggested a lesion of the cerebellum on the side of the nystagmus of greater amplitude. In these cases the findings were the result of direct or contrecoup pressure of the tumour locally on one lateral lobe of the cerebellum, and were probably aggravated by the presence of increased intracranial pressure.

(8) *Variations in the functions of the trigeminal nerve.*—Abnormalities of function of one or both trigeminal nerves were found in 25 per cent. of the cases studied. The changes varied from sluggishness of one corneal reflex and slight impairment of light tactile sensation on one side of the face to a definite impairment of tactile and pain sensation. In no case was sensation completely lost. It was more usual to find a distinct difference between the two sides with only moderate impairment of the finer variations on the affected side. As a rule, such changes were associated with similar changes in the limbs and trunk on the same side, but occasionally when the variations in sensation were slight the distribution of the trigeminal nerve alone was affected. In such cases a clear demarcation of the abnormal from the normal was

impossible. In only 7·5 per cent. did the tumour involve the parietal lobe at all; in 2·5 per cent. it had involved the temporal lobe; and in 15 per cent. it was entirely confined to the occipital lobe. In only one case was anæsthesia in the distribution of the trigeminal nerve associated with a spontaneous sensation of numbness.

(9) *Facial paresis.*—A suggestion of weakness of one side of the face was a common finding, and occurred in 57·5 per cent. of the cases under review. In no case, however, was a definite facial paralysis of either the peripheral or the central type found. In every case the suggestion of facial weakness was confined to the side opposite to that on which the tumour was situated. In 40 per cent. the weakness of the face was associated with indefinite or definite weakness of the arm and leg on the same side, and in several cases with abnormalities of sensation in the arm and leg on the same side. In others there was weakness of the arm and leg without any weakness of the face.

Such variations in facial weakness were comparatively slight—a difference in the naso-labial folds, a smoothing of one side of the face, or a slight lagging of one side of the face on voluntary movement. In others the face was smoother and flatter on one side than on the other, and the palpebral aperture on that side was narrower than normal. In others definite weakness of one side of the face at the angle of the mouth was evident on the patient showing the teeth or closing the eyes at command.

In 17·5 per cent. of cases, however, the emotional movements were affected as much as or more than the voluntary movements. The following are illustrative cases.

(1) In Case 3 there was slight weakness of the right side of the face on attempting to smile. On testing the facial muscles for voluntary movements, however, there was much less obvious weakness of the lower part of the right side of the face. The facial folds were greater on the right side of the face, but there were more wrinkles on the left side of the forehead. Associated with these findings there were also alexia, weakness of the right arm and leg, dragging of the right foot and a history of pins and needles, tingling and numbness in the right hand. The tumour occupied the left occipital lobe and encroached somewhat on the parietal and temporal lobes as well.

(2) In Case 9 there was slight weakness of the left side of the face only on emotional movement, together with weakness of the left arm and leg, and impairment of the sense of passive movement in the left arm and leg. The tumour was confined to the right occipital lobe.

In these cases the variations in the facial movements, whether confined to emotional movements alone or to emotional and voluntary movements together, were associated with evidence of involvement of the motor fibres in the corresponding arm and leg. It would appear, however, that when the involvement of the motor fibres is very slight the weakness of the face may be appreciated only on involuntary and emotional movements and give the impression that the paths for emotional movements are involved rather than those for voluntary movements. The conscious effort needed to initiate voluntary movements is enough to overcome the very slight weakness due to involvement of motor fibres so rapidly that delay in movement is not appreciated by the observer, whereas with involuntary movements some delay is at once noticeable. This observation does not necessarily contradict the belief that emotional movements are merely controlled by the more direct motor paths.

(10) *Involvement of other cranial nerves.*—The impairment of hearing which occurred in four cases was probably independent of the intracranial condition. In no case were the glosso-pharyngeal, vagus or spinal accessory nerves affected. A slight deviation of the tongue to one side was observed in some cases, but it was probably more apparent than real, as it was associated with slight weakness of the same side of the face and of the limbs on the same side.

(11) *Variations in the speech functions.*—Abnormalities of the speech functions were found on examination in 30 per cent. of the cases studied, and in 50 per cent. of those in which the left cerebral hemisphere was affected. No speech defect other than a transient difficulty was found in cases in which the right cerebral hemisphere was involved. Aphasia of some degree was present in 33 per cent. of cases in which the tumour was confined to the left occipital lobe, in 71 per cent. of cases in which the left parietal lobe was affected as well, and in 60 per cent. of cases in which both the left temporal and occipital lobes were involved. When the tumour definitely involved or approached the external surface of the left cerebral hemisphere, aphasia was present in 66 per cent., while in the remaining cases in which the tumour was confined to the middle or inner part of the occipital lobe, aphasia occurred in only ·9 per cent. It seemed, therefore, that either the speech areas or their connections had to be directly invaded by the tumour, or by œdema or vascular changes close to it, before permanent defects of speech appeared.

Nominal aphasia was found in 20 per cent., or in 33 per cent. of left-sided tumours; some form of visual agnosia in 22·5 per cent., or in 37·5 per cent. of left-sided tumours; and auditory agnosia in only one case. Other minor changes were found but were of little significance compared with the above abnormalities.

The types of speech defect found and their relation to the position of the tumour are illustrated by the following cases.

(i) In Case 3 the patient carried out movements correctly at command, but did not always obey the command at once. From time to time he perseverated. He read 11·53 as "seven min twel." He made no attempt to read or to spell words. When asked to name a series of objects he made fruitless attempts to recall the names. He knew the uses of objects and when he heard their names said "Yes" at once. A large tumour was removed from the outer aspect of the left occipital lobe and was found to involve the adjacent parts of the parietal and temporal lobes.

(ii) In Case 14 the patient had to be helped if he could not find the word he wanted. He could not name objects but could touch an individual object if it were named. He had some difficulty in reading written words. He could pick out objects when they were named and could write the names to dictation. A tumour the size of a hen's egg was removed from the subcortical part of the left occipital lobe close to the temporal lobe.

The presence of some degree of alexia was of considerable value in the localization of those occipital tumours which approached the external surface of the left occipital lobe. It was often associated with nominal aphasia.

(12) *Disturbances of sensation.*—Variations in sensation were present in 55 per cent. of cases. They were observed on one side of the body, not only in those cases in which the tumour had encroached on the part of the parietal lobe adjacent to the occipital lobe, but also in cases in which the tumour was confined entirely to the occipital lobe. They were, however, more common in those cases in which the tumour partly encroached upon the parietal or the temporal lobe. In every case they were confined to the side of the body opposite to that on which the tumour was situated. In some cases they were found over the face, arm, trunk and leg, while in others they were more or less confined to or more pronounced in the face, arm or leg. Occasionally, because of the impaired mental condition of the patient or of his difficulty in expressing himself, it was impossible to determine the degree of sensory impairment other than the changes in the cruder sensations.

Minor variations in sensation were the rule, while complete loss of sensation was not observed. Tactile stimuli and moderate differences in painful stimuli and between heat and cold were appreciated better on one side than on the other. In some cases these forms of sensation were merely impaired on one side when compared with the other, while in others there was a distinct difference in the responses when the two sides were stimulated. Various degrees of difficulty in appreciating the shape, size and weight of objects were observed. One patient was able to appreciate the weight of objects but could not be sure of their size. Slight difficulties were more common than complete loss of the power to distinguish the shape, size and weight of objects, though the latter did occur. Two-point discrimination and localization were impaired in all degrees, from a greater proportion of errors than on the other side of the body to complete loss of the power to localize a painful stimulus accurately. The sense of position and of passive movement were impaired in some cases, while in others there was impairment and sometimes loss of the power to appreciate vibrations when a tuning-fork was applied to the radius or malleolus.

When the appreciation of touch, pain and temperature were slightly impaired, the sense of position, two-point discrimination, localization and the appreciation of the shape, size and weight of objects were usually impaired as well. When, however, the latter group only were impaired, some were often affected and others normal. For example, in Case 25, in which the tumour was confined to the right occipital lobe, the patient had slight difficulty only in appreciating changes in position and passive movement in the left arm. In Case 26, in which the tumour involved the left occipital lobe and part of the parietal lobe, there was only some loss of the sense of position in the right arm. In Case 27, where the tumour affected the right temporal as well as the occipital lobe, the localization of painful stimuli was less accurate in the left arm than in the right arm.

In every case minor degrees of variation in tactile, pain and thermal sensations only were found, and in most cases localization, two-point discrimination, appreciation of slight changes in the position of the finger and toe, and the appreciation of variations in the size, shape and weight of objects were impaired rather than abolished.

The changes found were essentially those of involvement of the sensory paths above the level of the optic thalamus. With them was found in some cases difficulty in appreciating finer variations when a tuning-fork was applied to a bony prominence.

(13) *Motor abnormalities in the limbs.*—Motor abnormalities were found in the arm and leg in 90 per cent. of the cases studied. Minor degrees of muscular weakness, of alterations in muscle tone and of variations in the reflexes were the rule. It was difficult in many cases to decide what was the origin of the motor abnormality, and it was only after careful consideration of the distribution of the disability, the motor changes, the variations in co-ordination and the changes in the reflexes that an opinion could be expressed as to the nature of the motor change. In every case the following probable causes were considered: (*a*) Involvement of the motor fibres; (*b*) disturbance of cerebellar function on one side from direct pressure upon one lateral lobe of the cerebellum; (*c*) bilateral cerebellar dysfunction from a general increase in intracranial pressure; and (*d*) motor weakness from loss of sensation.

The comparative unimportance of cerebellar dysfunction from direct pressure as a cause of unilateral motor weakness was suggested by the fact that in practically every case the limbs affected were on the side opposite to that occupied by the tumour. Bilateral diminution of muscle tone with motor weakness and diminution of the tendon reflexes occurred in some cases in which the intracranial pressure was much increased. When such changes appeared after evidence of involvement of the motor fibres was already present, it was often found that the tendon reflexes on one side were absent while those on the other side were sluggish, the general diminution in the tendon reflexes probably being the result of the increased intracranial pressure and the sluggishness of the reflexes on one side due to the fact that the already exaggerated reflexes on that side persisted under such conditions. In other cases, definite variations in muscle tone and motor power, exaggeration of the tendon reflexes, diminution or absence of the abdominal reflexes and a doubtful or definite movement of dorsiflexion with the plantar reflex, left no doubt that the motor disability was the result of interference with the motor fibres. Occasionally a case was encountered in which no direct evidence of interference with the motor fibres or with the cerebellum was found to account for weakness of the contralateral arm and leg, whereas definite interference with sensory functions was evident and appeared to provide a satisfactory explanation for the weakness of the limbs and the difficulty the patient had in using them. While loss or diminution of tactile, pain and thermal sensation sometimes made the limbs clumsy and weak, it was usually when the sense of position was affected that the weakness of the limbs was most evident. This occurrence of motor disability with disturbance of sensation was regarded as analogous with that found when thrombosis of a branch of the middle cerebral artery had affected the posterior limb of the internal capsule, in which condition the resulting motor disability was often more disturbing to the patient than that associated with interference with motor fibres.

The above factors were evidently responsible for the motor disability in individual cases, and in some cases two or more of the factors were jointly responsible for the weakness of the limbs. The changes described in the following illustrative cases were characteristic of those occurring with tumours of the occipital lobe.

(i) In Case 2 the outstretched left arm tended to assume an abnormal attitude and fell away. The grip of the left hand was slow and weak. The finer movements of the fingers of the left hand were clumsy. The fingers missed an object more often with the left than with the right hand. There was slight weakness of the left leg compared with the right. Co-ordination was poor in both hands. On the left side the cremasteric reflex was sluggish and the plantar reflex was extensor. There was a well-marked flexion reflex on the left side. A tumour the size of a golf ball was removed from the upper and anterior part of the right occipital lobe. It reached the middle line and involved the adjacent part of the parietal lobe. In this case there was definite evidence of slight involvement of the motor fibres, probably by vascular changes or œdema in the neighbourhood of the tumour.

(ii) In Case 9 the left arm fell away on extension and was feebler than the right arm at every joint. There was sensory ataxia of the left arm. Hypotonia of the left arm was evident on passive movement and on hyper-extension. In the left leg tone appeared to be increased peripherally and there was inco-ordination with the heel-knee test. The tendon reflexes on the left side were slightly more active than were those on the right side. The sense of passive movement was impaired in the fingers and toes on the left side and later hypotonia was more pronounced in the left arm. The tumour occupied the right occipital lobe. In this case the extreme weakness and difficulty in using the left arm and leg could be explained satisfactorily by loss of the sense of position in those limbs and by the presence of sensory ataxia.

(iii) In Case 8 there was weakness of the lower half of the right side of the face for voluntary and emotional movements. There was slight weakness and increase in muscle tone in the right arm and leg. The tendon reflexes on the right side were more active than those on the left side, and the right plantar reflex was extensor. In walking, the patient dragged the right leg and failed to swing the right arm. Later there was definite nystagmus of wider excursion and more pronounced on lateral deviation of the eyeballs to the left. There was also severe hypotonia of the left arm, together with some decrease in tone in the right arm. The tumour occupied the left occipital lobe and was accompanied by a high degree of papillœdema.

In this case it was difficult to assess the relative importance of the different factors combining to produce the variations in motor function. At first there was evidence in the changes in the right arm and leg of interference with motor fibres, but the subsequent appearance of nystagmus and hypotonia on the left side was more difficult to explain. They may have been due to the increase in intracranial pressure, the muscle tone being reduced less in the right arm and leg because of the previous increase in tone due to the motor lesion. It was more probable that local pressure by the tumour on the left lobe of the cerebellum was aggravated by the general increase in intracranial pressure, and the preponderance of what were more or less definite signs of a cerebellar lesion on the left side produced in that way.

(iv) There were cases, however, in which the increase in intracranial pressure was apparently responsible for general muscular hypotonia and weakness, and even for the loss of tendon reflexes. Of this, Case 1 was an example. The knee-jerks were absent, while the right ankle-jerk was absent and the left present. Both plantar reflexes were flexor. Later, there was weakness of the right side of the face, and the right plantar reflex was sometimes extensor. During generalized convulsions the left arm and leg moved more than the right. There were seven dioptres of papillœdema in the right eye and six dioptres in the left. A large tumour occupied the anterior part of the right occipital lobe and the adjacent part of the temporal lobe. Here the general muscular hypotonia and the loss of tendon reflexes were probably the result of increase in the intracranial pressure and the persistence of a tendon reflex on one side due to a relative increase in tone on that side from slight involvement of the motor fibres.

From the cases examined it was evident that there was some difficulty in interpreting the disturbances of motor function associated with tumours of the occipital lobe. The motor changes were often slight, but, nevertheless, were often of much value in deciding upon which side the tumour was situated. There were, however, serious limits to their value, as was shown by the following case.

The patient, female, aged 19, was seen on February 22, 1930. She had had epileptiform attacks for nine years at intervals of about three weeks. These attacks were preceded by a strange feeling over the front of the head and in the epigastrium, but no visual symptoms were present. Twelve months before she was seen she had had "a nervous breakdown." On examination, the following positive findings were noted. The patient was mentally alert and co-operative, but obviously fatigued easily during the examination. Lateral deviation of the eyeballs to the right was defective, and attempts to deviate to the left resulted in a few irregular nystagmoid jerks. There was a definite left homonymous hemianopia with apparent spacing of the field for central vision. There were six dioptres of papillœdema in each eye. The right angle of the mouth was below the left at rest, and definite weakness of the lower part of the right face was evident on showing the teeth at command. There was a slight decrease in motor power and tone in the right arm compared with the left; and the motor power in the right leg was decreased compared with that of the left. In the arms the tendon reflexes were more active on the right side, the right abdominal reflex tired and disappeared before the left, and the right plantar reflex was probably flexor while the left was definitely so. There was a slight defect of localization of painful stimuli in the right arm compared with the left. There was a fine tremor of the fingers and repeated alternating movements were more awkward with the right arm than with the left.

In this case the signs in the right side of the face and in the right arm and leg suggested interference with the motor fibres in the left side of the brain, and it was only the definite left homonymous hemianopia which made it possible to localize the lesion in the right occipital lobe. The motor signs were probably false localizing signs which had developed after and because the intracranial pressure had been increased. At operation a large cyst was removed from the outer aspect of the right occipital lobe.

On the material studied the following conclusions as to the incidence and nature of motor changes in association with tumours of the occipital lobe appeared to be warranted.

(*a*) Minor disturbances of motor function occurred in practically all cases of tumour of the occipital lobe.

(*b*) The majority of them occurred in the contralateral limbs and as a rule were found to be due to involvement of the motor fibres by œdema or other changes in the tissues adjacent to the tumour. Changes due to involvement of motor fibres could, however, occur in the homolaterel limbs as false localizing signs due to and following an increase in intracranial pressure.

(*c*) Occasionally motor weakness in the contralateral limbs was associated with and probably due to loss of the sense of position.

(*d*) In some cases tumours of the occipital lobe were associated with general muscular hypotonia and motor weakness, probably because of of cerebellar dysfunction following the rise in the supratentorial pressure.

(*e*) In cases in which the factor mentioned above came into play the persistence of the reflexes in the contralateral limbs was probably due to interference with the motor fibres in the neighbourhood of the tumour.

(*f*) True cerebellar dysfunction affecting the arm and leg on one side was unusual, and when present may have been due to local pressure by the tumour or to local pressure aggravated by the increase in supratentorial pressure. Rarely there was a suggestion of cerebellar dysfunction affecting the contralateral limbs, which may have been due to a contrecoup pressure disturbing the contralateral lobe of the cerebellum.

V.—DISCUSSION.

Many of the clinical features of tumours of the occipital lobe have been discussed as they arose in the course of this paper, but certain general features of these lesions still remain to be considered.

The clinical course of the condition varied considerably. In some cases epileptiform attacks continued for as long as eight years before there arose symptoms or signs which more directly suggested the presence of an intracranial condition. In others, in approximately 57 per cent., general mental impairment, headache and transient or progressive failure of vision—symptoms suggesting a general increase in intracranial pressure—appeared early and the case ran its course in a few months. In these cases there was little doubt that the condition was symptomless until the onset of symptoms of increased intracranial pressure, a feature of more than half of the cases which made it very difficult to bring them under treatment before the more serious risks of increased intracranial pressure arose. The early appearance of symptoms suggesting the involvement of visual paths was unusual. Visual hallucinations occurred alone in only 2·5 per cent. and as the aura of an epileptiform attack in only 10 per cent. Epileptiform attacks appeared to be the most valuable of the initial symptoms in drawing attention to the presence of an intracranial condition as they occurred first in 30 per cent. of cases, in one-third of them with a visual aura and often as a few isolated attacks. It was apparent, therefore, that in only 10 per cent. of cases was it probable and in only 30 per cent. was it possible, to have the patient brought under treatment before the risks of increased intracranial pressure were incurred, and then only if a detailed examination of the nervous system were carried out.

When the patient came under observation the frequency of symptoms directly suggesting involvement of the visual paths was very little increased. By that time epileptiform attacks had occurred in 52·5 per cent., an unusually high figure compared with the average of 10 per cent. in an unselected series of intracranial tumours. The high incidence of other symptoms of increased intracranial pressure in association with such attacks—headache in 95 per cent., diplopia in 22 per cent., impairment of vision in 57 per cent., and disturbance of the sphincters in 12 per cent.—suggested that increased intracranial pressure was a factor of the greatest importance in the high incidence of epileptiform attacks. The higher incidence of epileptiform attacks in those cases in which the tumour had invaded the parietal or the temporal lobe as well as the occipital lobe appeared to be of importance only in so far as the extension of the tumour into those parts conditioned the occurrence of particular types of aura and the distribution of the convulsive movements.

Symptoms suggesting involvement of the central visual paths were limited to two—visual hallucinations and experiences suggesting abnormality of the visual fields. Visual hallucinations occurred in only 25 per cent. of cases. In 15 per cent. they were of an unformed type, which appeared to be due to an incomplete lesion close to the visual area of the cortex and such as might have resulted from early invasion of the optic radiations by tumour, by œdema or by vascular changes. Formed images, which occurred in 5 per cent., appeared to be the result of similar incomplete involvement of the visual paths in the anterior part of the occipital lobe and in the temporal lobe, where it was possible for a relatively large number of scattered fibres to be affected in such a way that the resulting stimuli were interpreted without difficulty as being visual stimuli arising through normal channels from formed objects external to the individual. Unformed hallucinations, therefore, seemed to be due to a lesion in the posterior part of the occipital lobe, while formed hallucinations suggested that the lesion was confined to the anterior part of the occipital lobe or had invaded the adjacent part of the temporal lobe. When sufficient information was forthcoming hallucinations were found to occur in the contralateral hemianopic field of vision, and were thus of some value in confirming the localization of the lesion when it affected the convex surface of the occipital lobe, especially on the right side in those cases in which no other definite localizing signs were found. In those cases in which the phenomenon occurred distortion of visual images was of some value in localizing the tumour in that part of the convex surface of the occipital lobe just anterior to the occipital pole. Experiences suggesting abnormality of the visual fields were rarely volunteered, but when described might have been of some help in determining the side upon which the tumour was situated in those cases in which it was no longer possible to confirm the information so gained by charting the visual fields.

Physical signs indicating involvement of central visual paths were confined to the information gained by charting the visual fields. It was possible, however, for a tumour of the convex surface of either the right or the left occipital lobe to be present without any distortion of the visual fields. When affecting the latter, disturbances of speech were usually of value in determining the position of the tumour, but when affecting the former it was possible for no localizing sign to be present. Actually, however, distortion of visual images owing to involvement of the visuo-psychic area or a history of unformed visual hallucinations due to the extension of œdema or vascular changes into the adjacent optic radiations, strongly suggested that in such cases the tumour affected the convex surface of the occipital lobe and in the absence of disturbances of speech favoured a localization in the convex surface of the right occipital lobe. No cases of tumour affecting the internal surface of the occipital lobe were found without some alteration of the visual fields, probably because the presence of the visuo-sensory area in the calcarine fissure and the inward course of the optic radiation towards this part and to the occipital pole made it improbable that a tumour could be for long in that region without interrupting the visual path.

A contralateral homonymous crescentic defect of the periphery of the visual fields, mentioned by Traquair [27] and suggested in one case by Bramwell [1], appeared to be confined to those cases in which the tumour was invading the occipital lobe from its convex surface. The essential feature of this type of visual field defect was the proportionate contraction of the contralateral temporal and of the homolateral nasal fields. It is probable that a tumour approaching the optic radiation from the outer aspect would affect first the fibres midway between the uppermost and the lowermost, and as it extended further interrupt more fibres above and below that level. That this type of field defect was produced in that way was suggested not only by the occurrence of cases in which only a peripheral crescentic contraction of the field was found, and of others in which the crescentic contraction of the field extended to within 20° of the fixation point, but also by the repeated observation of cases in which the contralateral temporal field became more and more contracted at successive examinations.

On the contrary, a tumour growing from the region of the falx cerebri into the internal surface of the occipital lobe appeared to have a greater chance of producing a contralateral homonymous quadrantic defect of the visual fields, especially if it were situated towards the upper or lower limit of the optic radiation. If only the upper or lower part of the visuo-sensory cortex in the calcarine fissure were involved early by a small lesion, a contralateral homonymous quadrantic defect of the visual fields would result. Invasion of the optic radiation slightly anterior to the visuo-sensory area of the cortex occurred in several cases and resulted in a similar homonymous field defect. In Weisenburg's [30] case a tumour invading one occipital lobe from the other in its anterior part produced homonymous hemianopia on one side and an homonymous quadrantic defect on the other side. Such a defect was possible if only the upper or lower fibres of the optic radiation were affected where they were arranged in a somewhat crescentic manner around the outer wall of the lateral ventricle. Similarly, a tumour deep in the anterior part of the occipital lobe could invade the lowermost fibres of the optic radiation as they passed upwards and backwards from the temporal loop and produce a contralateral homonymous quadrantic defect. The importance of these findings is the recognition of the fact that tumours affecting the lips of the calcarine fissure, those invading the internal surface of the occipital lobe just anterior to the calcarine fissure, and those deep in the anterior part of the occipital lobe can produce a contralateral homonymous quadrantic defect of the visual fields.

When the tumour arose in the part through which the optic radiation passed or extensively involved the optic radiation secondarily, a contralateral homonymous hemianopic defect of the visual fields with preservation of the field for central vision was found. It appeared that as long as a certain minimal number of visual fibres failed to be destroyed and the occipital cortex in the neighbourhood of the occipital pole was preserved, the field for central vision was unaffected. It seemed that for this to occur some stimuli for the cortical area for central vision in the neighbourhood of the occipital pole must have been conveyed by every corticopedal fibre in the optic radiation. It was possible, however, for the lesion to have destroyed those fibres passing to the calcarine cortex for peripheral vision and to have left those passing to the occipital pole unaffected.

Tumours large enough to have involved the greater part of the occipital lobe, those undergoing cystic degeneration, and those which infiltrated extensively the substance of the occipital lobe, produced a complete contralateral homonymous hemianopic defect up to the fixation point. In such cases, all of the fibres must have been interrupted.

The defects in the visual fields found in association with a tumour of the occipital lobe were thus shown to vary considerably with the position of the tumour and the degree to which it affected the fibres of the optic radiation. Quadrantic defects, usually described as characteristic of tumours of the temporal lobe, were equally probable with small tumours involving the calcarine fissure, and with large tumours invading the optic radiation from the inner aspect, or from below when situated in the anterior part of the occipital lobe. A tumour could be on the convex surface of the occipital lobe for a long time without producing any alteration in the visual fields, and one invading the optic radiation from the outer aspect could produce a slowly developing contralateral crescentic defect of the periphery of the visual fields. The frequent occurrence of a contralateral homonymous hemianopic defect with spacing of the field for central vision appeared to be due to preservation of fibres conveying stimuli for central vision, which may have been simply preservation of any of the fibres of the optic radiation; to destruction of those passing to the calcarine cortex and preservation of those passing to the occipital pole; or to destruction of the calcarine cortex and preservation of that at the occipital pole, together with preservation of many of the fibres of the optic radiation. A complete homonymous hemianopic defect up to the fixation point appeared to be due to destruction of all the fibres of the optic radiation; to destruction of the calcarine cortex and of the fibres passing to the occipital pole; or to destruction of both the calcarine cortex and that at the occipital pole with or without destruction of all the fibres in the optic radiation.

Neighbourhood symptoms and signs were found to be of considerable importance in cases of occipital tumour, not only in confirming the diagnosis of a focal lesion, but also in the detailed localization of the tumour. Only in the case of speech defects, however, did it appear to be necessary for the tumour to directly invade the adjacent parts, in order to produce the characteristic clinical features of a lesion of that part. Disturbances of the speech functions occurred in 50 per cent. of the cases in which the left occipital lobe was involved, and in 66 per cent. of the cases in which the tumour approached or involved the external surface of the lobe. Nominal aphasia, visual agnosia, and especially alexia, were of value in the localization of a tumour which had approached the external surface of the left occipital lobe, and in the majority of cases indicated definitely that the tumour was closer to the external surface than to the internal surface. Other neighbourhood symptoms and physical signs did not appear to have the same significance. Auditory hallucinations of the formed type and abnormal tastes and smells, which as a rule could not be identified, appeared to indicate disturbance of the functions of the temporal lobe, but owing to the position of the tumour in the cases in which they occurred, could not have been due to direct invasion of that lobe. Similarly, spontaneous subjective sensations in 30 per cent. of cases, and disturbances of motor function in 52 per cent., could have been the result in only a few cases of direct invasion of the parts by the tumour. While direct invasion of the central sensory paths by the tumour might have been responsible for spontaneous subjective sensations such as tingling, numbness and pins and needles in a few cases, in the majority they could not have been the result of direct involvement. In any case, this factor could not have accounted for the history of motor disabilities. When the results of physical examination were considered as well, it was found that sensory disturbances of a suprathalamic type and minor degrees of motor disturbances in the face, arm and leg of the opposite side were exceedingly common, the former in 52 per cent. and the latter in 90 per cent. The mild degree of these disturbances, their appearance in many cases shortly after symptoms of increased intracranial pressure had arisen, and the fact that they probably indicated involvement of structures in direct relation to the tumour itself, suggested that they were the result of œdema or vascular changes in the cortical and subcortical tissues of the post-central and pre-central parts of the parietal lobe on the same side as that on which the tumour was situated. Similarly, the symptoms already mentioned as indicating involvement of the temporal lobe were probably the result of the same mechanism.

Neighbourhood symptoms and signs of a different type were those which seemed to suggest involvement of one lobe of the cerebellum. While comparatively infrequent, giddiness, hypotonia in the homolateral limbs and nystagmus were common enough to be considered in the differential diagnosis of the condition. Though comparatively slight and indefinite in the presence of normal intracranial pressure, they appeared to be much aggravated when the intracranial pressure was increased. Such findings were probably the result of the direct transmission of pressure on to the lateral lobe of the cerebellum on the same side and were probably more definite when the intracranial pressure was raised because the increased supratentorial pressure transmitted through the tumour on to the lateral lobe of the cerebellum produced much more definite disturbances of cerebellar function.

Many of the clinical findings, however, which were likely to cause difficulty in diagnosis and localization were probably the direct or indirect results of increased intracranial pressure, whether due to secondary hydrocephalus or to œdema in the tissues adjacent to the tumour. General hypotonia and diminution of the tendon reflexes were probably the result of the direct transmission of the supratentorial pressure on to the cerebellum as a whole, while the apparent diminution in the muscle tone, motor power and reflexes on the homolateral side was often the result of the same mechanism, the difference in the findings on the two sides being due to involvement of motor fibres on the same side as the tumour. Similarly, indefinite nystagmus may have been due to the same mechanism or to mild degrees of weakness of one or both external recti muscles. Headache, papillœdema and transient or progressive failure of vision were definitely the result of increased pressure, while transient loss of vision in the hemianopic field was more probably the result of invasion of the central visual paths by œdema in the tissues adjacent to the tumour.

The disturbances of mental functions which were present in many cases were probably the result of one or both of two factors. In many they were undoubtedly the result of the disturbance of cerebral functions consequent upon the raised intracranial pressure and were more likely to appear when the pressure was raised rapidly; but in other cases it was evident that the presence of a tumour even in the occipital lobe was sufficient to disturb the normal cerebral associations enough to produce disturbances of memory and attention and to cause the patient to develop neurasthenic symptoms because of his impaired reaction to his environment. That such a factor as the latter came into operation in patients with tumours of the occipital lobe was of some importance when it was considered that such symptoms were often believed to suggest primary involvement of the frontal lobe by a tumour. That being so, early disturbances of mental function and neurasthenia might have been regarded as false localizing signs.

I. False localizing signs which actually led to an erroneous localization of the lesion were comparatively infrequent in the cases studied. It was apparent, however, that with tumours involving the convex surface of the occipital lobe and under conditions in which it was impossible to chart the visual fields there were many symptoms and signs which might have led to an incorrect localization. Symptoms and signs suggesting disturbance of cerebellar function and those indicating disturbances of mental function have already been mentioned. Formed visual hallucinations and abnormal tastes and smells might have suggested a lesion of the temporal lobe, spontaneous subjective sensations and disturbances of sensation of the suprathalamic type, a lesion of the post-central part of the parietal lobe, and minor degrees of motor dysfunction, a lesion of the precentral area, or of the corresponding frontal lobe when associated with even slight mental changes. In all such cases the chronological order of the appearance of the symptoms and physical signs was of supreme importance, if it were possible to determine it in detail, as it often was. Disturbances which appeared before the occurrence of one or more symptoms suggesting increased intracranial pressure were more likely to be due to a lesion of the part concerned with the functions disturbed, while those which appeared later were likely to be the result of the increased pressure. The appearance of symptoms suggesting a lesion of the temporal or of the parietal lobe at the same time as or shortly after symptoms of increased pressure might have been due to the extension of œdema about the tumour. If the increased pressure were due to secondary hydrocephalus, as it was in some cases, it was possible for the false localizing signs which developed subsequent to the rise in pressure to indicate a localization on the side opposite to that occupied by the tumour. This did not occur in any of the cases studied, but did occur in a case already quoted to illustrate this point. In this case the localizing signs mentioned appeared to indicate a lesion of the left parietal lobe, whereas the discovery of left hemianopia at an earlier stage and the displacement of a calcified area in the falx cerebri towards the left, showed that the actual lesion was not only in the right cerebral hemisphere but in the right occipital lobe. This opinion was confirmed at operation.

The relative importance of definite localizing signs, neighbourhood symptoms and signs, and the symptoms and signs of increased intracranial pressure in cases of tumour of the occipital lobe appeared to depend upon the correct appreciation of the time relations of the symptoms and signs, and upon the relative severity of the signs elicited. Distortion of the visual fields appeared to be the only sign upon which reliance could be placed and then only when incomplete or complete homonymous hemianopia was found. A contralateral homonymous crescentic defect of the visual fields was useful in localizing a tumour of the convex surface of the right occipital lobe, and appeared to be a sign worth searching for repeatedly in those cases in which symptoms of an intracranial lesion were present and no definite clue could be obtained to its situation. Neighbourhood symptoms and signs were of considerable importance in localizing the lesions, while those due to increased pressure were apt to be confusing and to lead to an erroneous localization if their true significance were not appreciated.

Apart from the differential diagnosis of tumours of the occipital lobe from tumours in other parts of the brain, the actual diagnosis of the presence of a tumour was often a matter of some difficulty. In many cases in which epileptiform attacks were a prominent feature, a detailed examination of the nervous system revealed findings which made it clear at once that an intracranial tumour was present. There were others, however, in which epileptiform attacks had occurred for some time and physical examination revealed no definite indication of the presence of a focal lesion. The only procedure possible in such cases was to regard the condition provisionally as idiopathic epilepsy and to re-examine the patient at intervals in the search for signs of a focal lesion. In this connection the examination of the optic discs and the charting of the visual fields appeared to be the most important.

The differential diagnosis from vascular conditions was never easy in the absence of unequivocal evidence of increased intracranial pressure. The difficulty was not, however, so common as might have been suggested by the absence of papillœdema or of other changes in the optic discs in 30 per cent. of cases. The diagnosis of a focal lesion and often the localization of the lesion itself were possible on the physical signs alone, while the slowly progressive nature of the illness with occasional exacerbations of headache, nausea, impairment of vision and clouding of consciousness appeared to offer direct evidence of a neoplastic rather than of a vascular lesion. Nevertheless, certain sources of confusion were evident. Homonymous hemianopia with sparing of the field for central vision could have been produced with equal facility by thrombosis of the posterior cerebral artery and by a tumour interrupting the visual path. Here again the manner of onset and the clinical history offered data upon which a differentiation could be made.

VI.—SUMMARY AND CONCLUSIONS.

(1) The clinical features of 40 cases of tumour of the occipital lobe have been reviewed, and their frequency, pathogenesis and significance discussed.

(2) The initial symptoms were epileptiform attacks in 30 per cent.; a visual aura or visual hallucinations in 12·5 per cent.; general mental impairment in 17 per cent.; headache in 35 per cent.; transient or progressive failure of vision in 15 per cent.; and strabismus in 2·5 per cent. In only 12·5 per cent. did the initial symptoms suggest that the visual paths were involved.

(3) The relative frequency of different symptoms of tumour of the occipital lobe was as follows: Visual hallucinations, 25 per cent.; symptoms suggesting abnormality of the visual fields, 16 per cent.; epileptiform attacks, 52·5 per cent.; auditory hallucinations, 5 per cent.; abnormal tastes and smells, 12·5 per cent.; headache, 95 per cent.; diplopia, 22 per cent.; impairment of vision, 57 per cent.; disturbances of speech, 35 per cent.; spontaneous subjective sensations, 30 per cent.; disturbances of motor functions, 52 per cent.; and mental symptoms, 55 per cent.

(4) Important findings on the examination of the patient were the following: Mental changes, 60 per cent.; contralateral homonymous defects of the visual fields, 94 per cent.; papillœdema or optic atrophy, 70 per cent.; inequality of the pupils, 35 per cent. (contralateral pupil the larger in 25 per cent.); ocular pareses, usually of the external recti, 30 per cent.; nystagmus and nystagmoid jerkings, 35 per cent.; disturbances of speech functions, 30 per cent. (50 per cent. of left-sided tumours); disturbances of sensation of the suprathalamic type, 55 per cent.; and minor degrees of motor disturbance usually in the contralateral limbs, 90 per cent.

(5) The changes in the visual fields found in the majority of cases occurred only in the contralateral halves of the fields. In individual cases the visual fields showed: (*a*) complete hemianopia up to the fixation point; (*b*) incomplete hemianopia with spacing of the field for central vision; (*c*) quadrantic defects; (*d*) peripheral crescentic defects; and (*e*) no abnormal changes. When vision was failing a concentric

contraction of the visual fields was sometimes found added to the above variations.

(6) An attempt was made to group the symptoms and physical signs as focal, neighbourhood and those due to increased intracranial pressure. Focal symptoms and signs were limited to unformed visual hallucinations and distortions of the visual fields. Neighbourhood symptoms and signs were of considerable importance in localization, and with the exception of disturbances of speech were probably the result of œdema or vascular changes in the neighbourhood of the tumour, or of pressure upon adjacent structures, sometimes increased by raised supratentorial pressure. Symptoms and signs resulting from increased pressure in some cases were confusing and increased the risk of an error in localization.

(7) In the majority of cases symptoms of increased intracranial pressure dominated the clinical picture from the beginning; in a few epileptiform attacks occurred for some time; and in others there was a history of exacerbations of increased intracranial pressure for as long as two years.

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NERVOUS AND MENTAL PHENOMENA ASSOCIATED WITH PAROXYSMAL TACHYCARDIA.[1]

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INTRODUCTION.

It is my purpose here to call attention to the various nervous and mental manifestations which may be associated with paroxysmal tachycardia. Neurologists or psychiatrists are prone to consider tachycardia as belonging to the domain of the general physician, and as a consequence to overlook a syndrome that frequently has distinct nervous or mental phenomena associated with it. These phenomena may be so marked and may present such a variable picture as to mask the underlying cause, giving rise to many misconceptions and leading to incorrect diagnosis. The literature on paroxysmal tachycardia is voluminous, but comparatively little has been written regarding the nervous and mental aspects of the problem. As far as I know, no one has assembled the observations of physicians of the past who noted nervous or mental elements in the syndrome of paroxysmal tachycardia.

HISTORY.

Galen, in "De Pulsibus," mentioned sudden paroxysms of palpitation in young persons of apparently perfect health, not infrequently terminating fatally by syncope. In Wood's "Practice of Medicine," 1852, a most accurate description of paroxysmal tachycardia is given and the condition is recognized as being functional. Von Bamberger, in his "Lehrbuch," commented on the syndrome and mentioned the occurrence of headache, dizziness, scotoma, tremor, and even unconsciousness in the attacks.

From these early and somewhat vague references one may turn to the year 1867, when, within a brief period, four writers published reports of cases in the *British Medical Journal* on "Unusually Rapid Action of the Heart." In a case reported by Cotton, a patient had associated sensations of faintness, and in a case reported by Watson

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the patient died in his fourth attack. In spite of these reports, little of special interest appeared until 1874, when Huppert described the condition but stated incorrectly that previous reports had not appeared in the literature. Proebsting, in 1882, was more fortunate and, besides describing three cases of his own, was able to review reports of numerous cases from the literature. A few years later Bristowe made several pertinent observations. He noted that as far as the heart is concerned the condition is functional, and if any cardiac disease is present it is purely accidental.

It remained, however, for Bouveret, in 1889, to realize the significance of the syndrome, and he coined the term "tachycardie essentielle paroxystique." He published an exhaustive and masterly review of the subject and left comparatively little to add other than details, reports of unusual cases and the more recent and important electrocardiographic studies. He fully appreciated the significance of associated cerebral phenomena and attributed them to ischæmia or cerebral circulatory changes. It is strange that Bouveret's work made but slight impression at the time, and approximately ten years elapsed before any noteworthy contribution was published, although occasionally case records appeared under the heading of cardiac neurosis, cardiac epilepsy, and even under the heading of gastric neurosis.

Herringham, in 1897, reviewed reports of fifty-three cases gathered from the literature. He pointed out that there was no essential difference in the cases of organic cardiac disease, and that Bouveret was not justified in excluding such cases. He also recognized various cerebral manifestations and mentioned, in particular, one case from the literature in which the attack was initiated by loss of consciousness..

Schlesinger was the first to make a thorough study of paroxysmal tachycardia in relation to the central nervous system. He studied fifteen cases, and noted a great variety of neurological manifestations. He observed that in spite of marked tachycardia the patients usually were able to carry on their accustomed physical duties. He emphasized the fact that in the majority of cases careful clinical study did not reveal organic disease, and that, beyond the cardiac condition, evidence of neurosis could not be established. Unlike most observers, however, he noted that neurasthenia or hysteria might be associated, although such states were rather the results of the tachycardia than the cause. Schlesinger observed paroxysmal tachycardia in a patient subject to Quincke's œdema, and it was his belief that the œdema played a causative part in the production of the tachycardia. He also noted the association of unconscious attacks with paroxysmal tachycardia, and reported four cases in which attacks of paroxysmal tachycardia were initiated by a convulsive attack and unconsciousness. In one of these cases, circumscribed œdema was always present with an attack and never occurred between attacks. He suggested that possibly the convulsive attacks in this case were due to œdema of the cortex, for not infrequently convulsive attacks are associated with circumscribed œdema. He was able to find, in the literature, reports of ten cases of paroxysmal tachycardia with convulsive seizures, and in the majority of these cases he assumed the convulsions to be due to cortical œdema, vascular spasms, arteriosclerosis, or some other cerebral factor. Although the term " cardiac epilepsy " has been employed, Schlesinger did not consider paroxysmal tachycardia as an epileptic equivalent. He stated, however, that the more one studies paroxysmal tachycardia, the more tenable the theory of an epileptic factor seems to be.

As might be anticipated, every writer on the subject had some favourite mechanism to propound as the cause of paroxysmal tachycardia, but the consensus of opinion regarded it as a neurosis. The occasional association of migraine prompted the idea of an underlying migraine or gouty diathesis. Thomas and Post suggested that paroxysmal tachycardia might be the cardiac manifestation of migraine.

It is impossible to review all the hypotheses applying to the causation of paroxysmal tachycardia. The very fact that there was no unanimity of opinion lends weight to the conclusion that much was left for the future.

With the advent of the electrocardiograph added light was thrown on paroxysmal tachycardia. In 1924, Willius and Barnes presented an exhaustive and careful study of the subject. They classified tachycardia into (1) simple (nodal, auricular, ventricular), (2) auricular fibrillation, and (3) auricular flutter. In a supplementary study Barnes called attention to various cerebral manifestations of the disorder and reported several interesting cases.

DEFINITION.

Paroxysmal tachycardia may be defined as a condition which is characterized by the following features: (1) Sudden change in the normal cardiac mechanism, producing a rapid rate, varying between 120 and 250 beats a minute; (2) the patient may or may not be entirely conscious of the great degree of cardiac acceleration; (3) the attack generally covers a definite period of variable length, from minutes to hours, or even, rarely, days; (4) the tachycardia not only begins abruptly but usually ends abruptly; and (5) cerebral phenomena may be associated with the attack and may tend to dominate the clinical picture.

ÆTIOLOGY.

Paroxysmal tachycardia is slightly more prevalent in males than in females. It may occur at practically any age, ranging from 7 to 70 years. It is, however, comparatively rare in children. Willius found reports of only twelve authentic cases in childhood, and added one of his own, that of a girl aged 7. The greater number of patients present themselves between the fourth and sixth decades of life. As a rule the attacks continue over a period of many years. Hoffmann reported one case in which the attacks had existed for fifty years. I have seen several cases in which it had existed over a period of thirty years. As a rule the attacks vary considerably as to frequency. There may be recurring attacks for several months, or even years, and then there may be a free period of months or years. Again, a patient may have an attack once or twice a year, over a long period of time. Although previous diseases, such as tonsillitis, influenza and rheumatic fever are frequently recorded, it must be admitted that the percentage is hardly sufficient to warrant a positive deduction. Exciting causes are numerous and belong to the conditions usually associated with functional disorders, such as emotional disturbances, exertion (such as dancing and skating), ingestion of food, flatulence, sudden change in posture, excessive use of tobacco or alcohol, and prolonged pain; at times percussion over the heart will precipitate an attack. The attacks may, however, have no apparent exciting factor and may occur without warning and even during sleep.

MORBID ANATOMY.

The outstanding factor in the pathology of paroxysmal tachycardia is the absence of organic changes. From very early times efforts have been made to single out some cardiac or extracardiac lesion which might be a factor in the production of the disease. Schlesinger reported a case in which at necropsy compression of the right vagus nerve was found. Since his observations several others have reported similar lesions, but when the evidence for a lesion of the vagus nerve, as a cause of tachycardia, is summed up, there is comparatively little basis for a conclusion. Reinhold, in 1906, reported a case in which there was syphilitic basal meningitis, and one in which there was a tumour of the left cerebellum, but he himself concluded that these lesions might be wholly unrelated to the tachycardia. It is unquestionable that, in the presence of pathological changes in the heart, the condition takes on a more serious aspect, but pathological change in tissue is contributory, not primary. Summing up the evidence at hand, one must conclude that up to the present time pathological investigation has not revealed any single factor of positive value. Yater, in a study of the pathologic changes in arrythmia, studied 154 hearts without finding any specific histological lesion to account for the tachycardia.

Nervous and mental symptoms are probably secondary to interference with the normal cerebral circulation. Owing to the rapid beat of the heart, the ventricles fail to fill properly, and as a result the volume of the flow of blood to the brain is decreased, resulting in symptoms usually attributed to cerebral anæmia. The presence of arteriosclerosis naturally would serve as an added factor in producing circulatory changes during an attack, and may in part account for cerebral manifestations occurring more commonly in adults.

SYMPTOMS.

The clinical picture of paroxysmal tachycardia is so characteristic and so fully described by its definition that it does not need detailed description. The important point from the standpoint of the physician is to keep the condition in mind, and in the presence of recurring, unexplained cardiac or cerebral phenomena to question closely concerning the exact symptoms. If need be, he should endeavour to witness an attack; also, if possible, he should obtain an electrocardiographic tracing during the attack. Lewis has pointed out that the less frequent the attacks the longer they last. In any given patient the duration of attacks is fairly constant, so that the individual paroxysms are similar.

As a rule the patient suddenly becomes aware of cardiac palpitation, the heart may seem to turn over or "flop over" and race off at a rapid rate. Often the attacks are of short duration, and the patient may continue with the usual work without especial embarrassment. Lassitude, exhaustion, sweating and even prostration may supervene. Throughout the attack the cardiac rate remains the same, and as a rule cessation is as abrupt as the onset, although gradual subsidence not infrequently occurs. Within a brief interval the patient regains his normal composure and status, although general lassitude may persist for several days. As a rule, the patient does not seek advice with a first attack. The tachycardia may go unnoticed for years and may be considered as some trouble not cardiac in origin.

DIAGNOSIS.

The diagnosis of paroxysmal tachycardia is comparatively simple if the condition is kept in mind. The difficulty is that only too often the patient is not seriously impressed by the tachycardia but regards the cardiac activity as secondary to dizziness, faintness or some factor in the condition. On the other hand, many of these patients live in dread of recurring attacks, and as a result definite anxiety neurosis develops, so that one may have considerable trouble in appreciating the existence of two separate syndromes. Because of the variable associated phenomena, many of these cases are incorrectly diagnosed as vertiginous attacks, neurosis (cardiac, anxiety, gastric and menopause), *petit mal*, syncopal attacks, epilepsy, chronic nervous exhaustion and migraine-epilepsy complex.

Naturally, many of these cases are classified under the heading of cardiac neurosis. Hirschfelder has attempted to differentiate the purely neurotic type of case and the essential or myogenic type on the following basis: In the neurogenic type the tachycardia sets in gradually and subsides gradually, whereas in the myogenic type it sets in at a single leap and the heart-beat reaches its maximal rate within one or two cardiac cycles. Willius, in considering cardiac neurosis, stated that many cases of paroxysmal tachycardia are neurogenic in origin, and that paroxysmal nodal tachycardia is the type that is most frequently neurogenic. He has never observed paroxysmal auricular fibrillation, auricular flutter or ventricular tachycardia in hearts not affected by disease.

In some instances a differential diagnosis is not easy; thus, one patient may present gastric complaints, such as recurring attacks of flatulence associated with dizziness and vertigo. Closer examination reveals the fact that the condition is entirely cardiac but the patient has misinterpreted his own sensations. In any given case, if doubt exists, a final opinion should not be rendered without electrocardiographic study.

Barnes obtained electrocardiograms in thirteen cases during attacks; the origin of the tachycardia was as follows: in seven, nodal; in three, ventricular; in one, auricular; and in two, auricular flutter.

In patients who present syncopal attacks, or unconsciousness, it is easily seen that at times distinction between paroxysmal tachycardia and epilepsy is difficult. In paroxysmal tachycardia there is usually a warning and the patient frequently is able to prevent the attack by lying down. If unconsciousness supervene the patient rarely falls, but tends to slide to the ground. There is absence of convulsive movements, although, in the excitement, a few movements of the patient may be recalled by the witnesses as convulsive acts. Sphincter disturbance is absent, and on recovery, even though there be exhaustion, stupor or sleep is absent. True convulsive seizures also may occur, but they are comparatively rare, and unless distinctly associated with an attack of tachycardia must be considered as an independent condition. As a rule, in epilepsy the patient becomes cyanotic, whereas in paroxysmal tachycardia he becomes pale. A distinguishing feature in paroxysmal tachycardia is the fact that after the attack has begun, change in posture does not affect the cardiac rate. As a rule, in physiological acceleration, as in exophthalmic goitre and infectious processes, the rate responds to rest and postural changes. Vomiting, prostration, or even delirium must be recognized as occasional phenomena associated with paroxysmal tachycardia. It should be kept in mind that persistent tachycardia, in which the cardiac rate is 140 or more, and in which this rate is maintained in a variety of circumstances, is almost always due to a new and pathological heart rhythm [15].

NERVOUS AND MENTAL PHENOMENA.

The recorded frequency of nervous and mental symptoms in paroxysmal tachycardia depends on the investigator's attitude in including mild symptoms, such as anxiety, dizziness and vertigo, as part of the syndrome. In about 20 per cent. of cases of paroxysmal tachycardia in the Mayo Clinic, mental phenomena of varying degree are encountered. Definite nervous manifestations are somewhat less common; they occurred in the same group of patients in about 15 per cent. of the cases, the symptoms varying from mild dizziness to attacks of unconsciousness. In spite of the rather infrequent occurrence of mental disturbances, it is noteworthy that many patients are entirely free of associated psychotic disturbance and have learned to accept their attacks without any marked concern.

The more common disturbances referable to the nervous system may be grouped as nervous and as mental phenomena. Nervous phenomena are dizziness, vertigo, syncopal attacks, visual disturbances such as temporary blindness and scotoma, attacks of unconsciousness, convulsive seizures, paræsthesia, pain and transitory aphasia. Among the more common mental phenomena associated with the attacks of paroxysmal tachycardia are anxiety, depression, agitation, mental and physical exhaustion, rarely mild delirium, and at times hysterical manifestations.

These associated phenomena are not confined to any special age. They appear more often in cases in which the origin of the stimulus and the propagation over the heart shows the greatest deviation from normal. Thus, Barnes found that cerebral manifestations were present in 60 per cent. of cases of paroxysmal tachycardia in which the impulse originated in the ventricle; in 41 per cent. of the cases there was nodal tachycardia; in 25 per cent. auricular tachycardia, and in 6 per cent. auricular flutter. As far as can be determined, the occurrence of cerebral manifestations does not affect the prognosis in paroxysmal tachycardia.

The exact relationship of nervous or mental symptoms to the attack of tachycardia is extremely variable. Occasionally the attacks are ushered in by some symptom such as depression, anxiety, vertigo, or even unconsciousness, so that the entire attention of the patient is focused on the initial symptom and the underlying condition is not recognized and in itself causes no concern.

Frequently patients with paroxysmal tachycardia are treated for nervousness, and for years the condition may be classified under the heading of cardiac neurosis, anxiety neurosis, chronic nervous exhaustion, menopausal neurosis, and so forth. In any given case, if there are any associated disturbances with the attack they tend to remain more or less constant. Thus, a patient with fainting attacks will continue with variable degrees of syncope, and a patient with paræsthesia will continue to have paræsthesia.

That psychic factors may play an important part in the causation of attacks is undoubtedly true. Kuré, in a study of the psychic manifestations, was able to show that psychic influences, such as working out mathematical problems under strain and stress, might precipitate an attack. It is because of this frequent psychic association that in many cases the diagnosis of anxiety neurosis is made.

PROGNOSIS AND TREATMENT.

Barnes, in a previous study, pointed out that the prognosis in cases of paroxysmal tachycardia, without signs of organic cardiac disease, is good, and that the attacks are compatible with long life; but if attacks occur in conjunction with organic cardiac disease, the prognosis is determined by the type and degree of the underlying cardiac injury. Since, in the majority of instances, there is no pathological change in the heart, one is justified in assuming a favourable prognosis as far as life is concerned. The duration of the disease is extremely variable. At times a few isolated attacks conclude the picture. More often the condition tends to recur over many years; the average duration, at the time the study was made, was about ten years. I have seen several cases which have extended for more than thirty years, and some writers have reported cases of fifty years' duration. That the condition must not be treated lightly is evident from the fact that I have seen death occur as a result of a paroxysm in a case in which no cardiac or other pathological cause of the condition could be found. One woman, aged 23, died during an attack, and at necropsy chronic fibrinous myocarditis, dilatation of the left ventricle, a defect of the intraventricular septum, and an aneurysm were found. There is nothing in the association of nervous or mental phenomena which alters the prognosis. However, nervous and mental changes are more prone to occur in those cases in which there is a definite cardiac lesion. Attacks of paroxysmal tachycardia also may prove serious or even fatal if associated with pulmonary disease. I have had one patient who died in the course of post-operative bronchopneumonia, but death occurred as an immediate sequel of an attack of tachycardia.

Of paramount importance in the treatment of paroxysmal tachycardia are the recognition and treatment of any pathological change in the heart. Whether or not there be a cardiac lesion, the patient must fully appreciate the nature of his condition, for there is little doubt that emotional strains and stresses do precipitate attacks. The elimination of toxic agents, such as alcohol and tobacco, is important, for not infrequently the reduction of smoking alone may lessen the frequency of the attacks. With the onset of the attack complete rest and relaxation may shorten or may even abort an attack. Vagal pressure, or the production of vomiting, may abort an attack; patients frequently learn to induce vomiting to relieve the condition. In several instances the removal of foci of infection, such as the tonsils, has seemingly been of value. Morphine sulphate rarely does much good unless it produces vomiting, and naturally, in recurring attacks, its use is contra-indicated. Digitalis is of no value. Quinidine sulphate given in doses of 3 to 4 gr. (0·20 to 0·24 grm.) every three or four hours during the day and night appears to be the most helpful remedy, as it tends to depress the irritability of the auricle. If the attacks are frequent, the quinidine may be given in doses of 3 gr. (0·20 grm.) three to four times a day over an indefinite period of time. Finally, all emotional strains and stresses should be eliminated from the life of the patient.

CASES ILLUSTRATING THE MORE COMMON NERVOUS AND MENTAL PHENOMENA.

Case 1. *Paroxysmal nodal tachycardia with vertigo.*—A man, aged 62 years, had been subject to severe attacks of vertigo for the last four years. He recalled, only after direct questioning, that these attacks had been attended by sudden seizures of tachycardia. The Wassermann reaction of the blood was positive, and signs of syphilitic aortitis were present. A radial pulse could not be obtained in the right arm, but collateral circulation was well established. There was marked arteriosclerosis. After the patient had been under observation a few days severe vertigo developed. The pulse-rate was 160, and an electrocardiogram taken during the attack identified the paroxysm as nodal tachycardia with a pulse-rate interval of zero and a cardiac rate of 150. The vertigo ceased when the heart resumed its normal rate.

Dizziness or vertigo is one of the most common associated nervous manifestations encountered in paroxysmal tachycardia. This case is selected because of the electrocardiogram. As far as could be determined, syphilis did not play a part in the causation of the attacks. The patient has now been under observation for five years, and at the age of 67 remains in fair health and only rarely has an attack of tachycardia.

Case 2. *Paroxysmal tachycardia with syncope and loss of consciousness.*—A nurse, aged 22, five years before she came to the clinic had begun to have what she considered to be fainting attacks. At first they occurred infrequently, but for fourteen months had been coming on about every six weeks. A diagnosis of epilepsy had been made. The attacks usually had come on while the patient was working hard or was under strain. Suddenly a peculiar sensation would pass over her, the heart seemed to stop for a moment and then beat rapidly. With this a feeling of weakness and faintness came on, and unless she could lie down or get fresh air, she would sink to the floor and might be unconscious for a moment, or as long as fifteen minutes. She was observed in one attack; the rate of the heart was about 200 for about an hour and a half; then, suddenly, it returned to normal. Following an attack there was a sense of exhaustion lasting for several hours.

In this case the dominant feature was the loss of consciousness. The result was an erroneous diagnosis of epilepsy.

Case 3. *Paroxysmal tachycardia with convulsions.*—A woman, aged 50, had begun to have attacks of unconsciousness thirty years before she came to the clinic. The attacks recurred several times a year. Suddenly she would feel dizzy and weak, and, unless she could get to a chair, would fall unconscious.

She never had had any convulsive movements, but she sometimes became rigid. Attacks occurred at night, and she awoke with the onset. The attacks always began with sudden onset of rapid heart-rate, a cold sensation passed about the mouth, and the lips tingled, objects grew dark before her and syncope followed. Attacks lasted from a few minutes to seven hours.

In this case a diagnosis of epilepsy had been accepted for a long time, and it was only on very close questioning that a history of cardiac abnormality was obtained, as all previous interest had centred about the convulsions. In spite of the long history, the attacks are now less severe and there is no indication of mental deterioration.

Case 4. *Paroxysmal tachycardia associated with syncope and unconsciousness.*—A clergyman, aged 43, twenty years before he came to the clinic had begun to have attacks of tachycardia lasting about a half hour. Usually the attacks had been brought on by exertion, but also occurred without apparent cause. Seventeen months before he presented himself for examination, he suddenly had had an attack while preaching, had become weak, had fallen and had been unconscious for five minutes. Seven months later a similar attack had occurred. In the last five months he had had four attacks. The attacks were usually preceded by a depressed feeling, discomfort in the epigastrium, and then the sudden appearance of tachycardia. If he could sit or lie down he could usually ward off the attack. If he were unable to ward off the attack, the heart-rate continued at about 200 beats a minute until he sank to the floor and remained unconscious for five to ten minutes. Following an attack he was weak, but not sleepy. He experienced some anxiety during the attack, but anxiety did not precipitate an attack.

The first impression was that the cause of the condition was epilepsy of the *petit mal* and *grand mal* types. The patient also was rather markedly anxious and depressed as the result of these attacks, but as far as could be determined the anxiety did not precipitate attacks.

Case 5. *Paroxysmal tachycardia with anginoid type of pain.*—At the age of 17, following influenza, a woman began to have infrequent attacks of tachycardia. At the age of 45 the attacks had become more severe, lasting from two to thirty-six hours. Since the onset of the tachycardia she had been subject to pain running down the left arm, especially in the region of the deltoid muscle and at the elbow (not ulnar distribution). On a few occasions she had had contraction of the hands and feet, simulating tetany. During an attack she had a heart-rate of 200. An electrocardiogram taken during an attack showed premature T-waves in leads I and II, and inverted T-waves in lead III. The Q.R.S. interval was at the upper limit of normal.

In this case the possibility of true organic disorder was naturally the first consideration. The pain, however, was not typical of true angina, and when considered as part of the paroxysmal tachycardia, the syndrome justified an entirely different prognosis from that of severe organic cardiac disease.

Case 6. Paroxysmal tachycardia with visual disturbance and symptomatic depression.—In 1905, when the patient, a man then 38, was at work, suddenly everything grew dark before his eyes and he had a sensation as of "stars falling" before his eyes. He slowly fell forward, but saved himself and sat down for several minutes. He had been aware of marked tachycardia and dyspnœa. In 1915 he had had a similar attack that had been followed by weakness and depression for several days. A physician had told the patient at this time that his heart was "very bad," and that he would "fall over some time and forget to wake up." No further attacks had occurred until 1919, when the trouble had returned. In this attack at this time he sank to the ground, but was not convulsed. Since then up to the time of a visit in May, 1928, he had had, on an average, three or four attacks a year, lasting from three to ten minutes each. Following attacks he had been depressed and had dreaded not being able to do his work, everything had seemed wrong, words had confused him and he had been unable to do his usual work. He had had similar depression without attacks of tachycardia, but invariably had become despondent with an attack. Examination had been entirely negative in 1921 and was negative again in 1928.

Visual disturbances are not uncommon in paroxysmal tachycardia and may vary from momentary blankness to marked scotoma. In this case the depression may have been provoked by an unwise remark on the part of the physician.

Case 7. Paroxysmal ventricular tachycardia with blindness.—A man, aged 34, complained of attacks of vertigo and blindness, followed by rapid action of the heart. The attacks had begun two months before his visit to the clinic. The patient used tobacco and coffee to excess. He suffered from migraine, but there was no relation between the headaches and the attacks of rapid action of the heart. In a typical attack he first became totally blind and dizzy for a few seconds, after which "the heart ran away with itself." He felt weak during the attack, was pale and bathed in cold perspiration. The attacks lasted about four hours and ceased after he had vomited. The electrocardiogram taken during an attack gave evidence of ventricular tachycardia with a rate of 257. General examination gave negative results, except for infected tonsils, which were removed. Three years later the patient was free from attacks, and from symptoms of myocardial failure.

The possibility of a migraine equivalent was considered but could not be established. The removal of the infected tonsils and limitation of indulgence in tobacco and coffee may have been factors in improvement.

Case 8. *Paroxysmal tachycardia, with paræsthesia and aphasia.*—A woman, aged 33, had had enlargement of the thyroid gland since the age of 17. Since influenza in 1919, she had not been well and had been nervous and easily exhausted. About a year before she came to the clinic she had begun to have attacks which always had started with sudden onset of rapid action of the heart. Prickling and numbness about the mouth and of the hands and feet followed an attack. For five to fifteen minutes she felt helpless and unable to talk. Following the attacks she was exhausted. The attacks were brought on by worry, nervous strain, or quarrels.

Paræsthesia is a rather common manifestation of paroxysmal tachycardia and may be of varying degree.

Case 9. *Paroxysmal tachycardia; nocturnal attacks; syncope associated with unconsciousness.*—A man, aged 38, five years previous to his visit to the clinic had begun to have sudden attacks characterized by rapid beating of the heart, paræsthesia, and twitching of the left arm. The attacks occurred about monthly, and lasted from three to ten minutes. On two occasions they had been associated with loss of consciousness. The attacks occurred at night, waking him out of a troubled sleep. In the convulsive attack his limbs were contracted, but clonic movements had never been present. A diagnosis of epilepsy had been made.

The occurrence of attacks at night is not common; it need not be interpreted as a sign of epilepsy. The character of the convulsions was not epileptic, and there were no features in the case to suggest a localized cerebral lesion.

SUMMARY.

The syndrome of paroxysmal tachycardia is one that has long been recognized by general physicians, but that has been given little consideration by neurologists and psychiatrists. There seems little doubt that nervous and mental phenomena are frequently associated symptoms and that they may so dominate the picture as to lead to incorrect diagnoses. Although emotional elements may play a part in the syndrome they may be entirely absent, and the symptoms are then directly the result of a cerebral vascular change. It is therefore advisable, in the presence of any recurring paroxysmal type of attack, to bear in mind the possibility of paroxysmal tachycardia and its associated phenomena.

CONCLUSIONS.

(1) Paroxysmal tachycardia is of fairly common occurrence, and because of its associated nervous and mental manifestations merits the consideration of neurologists and psychiatrists.

(2) Its chief characteristic is its abrupt onset and cessation.

(3) It is more common in neuropathic persons, and there may be other evidence of functional nervous disturbances.

(4) The presence of organic pathological changes in the heart need not modify the clinical picture, although the prognosis varies with the degree of cardiac injury.

(5) The nervous and mental phenomena may vary from slight anxiety or dizziness to delirium or convulsions.

(6) Although it is not possible to establish either an isolated ætiological factor or a precise pathological lesion, paroxysmal tachycardia represents a clinical entity and should be so recognized.

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NOTICES OF RECENT PUBLICATIONS.

Encephalitis im Kindesalters. By A. ECKSTEIN. S. 172. Berlin: Julius Springer. 1929. Price M. 12.

In view of the interest evoked to-day by the acute cerebral complications of the exanthemata and by other types of encephalitis, the appearance of Dr. Eckstein's monograph is particularly opportune. The author discusses fully the clinico-pathological aspects of that broad group of cases occurring in childhood in which acute cerebral manifestations occupy the foreground of the clinical picture, whether complicating some systemic disease or arising spontaneously. Naturally a large proportion of the monograph is concerned with the symptomatology of acute and chronic epidemic encephalitis. Epidemic forms of encephalitis, other than encephalitis lethargica, are next considered. Within this category, Eckstein includes the cases of "acute serous encephalitis," reported from Boston and New York by Brown and Symmers; the Japanese epidemic described by Kaneko and Aoki; the cases of Stoos; and lastly, the "X disease" of Australia. Thereafter, the sporadic cases of encephalitis in childhood are described, illustrated by a long series of the author's personal cases. "Para-infectious" encephalitis is considered in some detail, followed by a careful study of post-vaccinal encephalitis. A useful table is given, setting out the particulars of ninety-three examples reported in Germany, including three patients from the author's series. Altogether, this monograph constitutes an able and readable presentation of the subject, and is printed and illustrated in the excellent manner which characterizes Springer's publications.

Tumeurs médullaires associées à un Processus syringomyélique. Par N. JONESCO-SISESTI. P. 295. Paris: Masson et Cie. 1929. Price 45 frs.

The rare but interesting condition in which an intramedullary tumour of the spinal cord is associated with syringomyelic lesions above and below the level of the growth is carefully studied from both its clinical and anatomical aspects in this monograph. The author had the opportunity of observing several cases under Professor Guillain, and he has also collected many others from the literature. From an analysis of these cases he concludes that sensory symptoms generally appear first and are usually the most prominent throughout the course of the illness. The earlier disturbances are generally radicular in distribution, but later they are more widespread. For a time the characteristic syringomyelic dissociation of sensation is found, but tactile sensibility diminishes rapidly. The motor symptoms are less characteristic, and, as the sensory, tend to vary from time to time.

The author emphasizes the importance of an examination of the cerebrospinal fluid, for though the typical Froin syndrome is usually present the cerebrospinal pressure is not raised. The primary tumours are classified as fibrogliomata, ependymogliomata, and complex tumours, chiefly teratomata, while the syringomyelic lesions are attributed to a gliomatosis which originally surrounds the tumour but later spreads throughout the cord.

Spezielle Histopathologie des Grosshirns. Von Professor Dr. A. JAKOB. Erster Teil, mit 266 zum Teile farbigen Abbildungen im Texte. S. 412. Leipzig und Wien: Franz Deuticke. 1929.

This valuable addition to Aschaffenburg's "Handbuch der Psychiatrie" deals with the special histopathology of the brain, and is as trustworthy and informative as its author's reputation would lead one to expect.

After an introduction in which the problems and limitations of research in this field are discussed in a temperate and comprehensive way, there is a section on tuberculosis of the brain and its membranes. The body of the book is devoted to syphilis, considered under five heads: syphilitic meningitis and meningoencephalitis, vascular lues of the brain, cerebral changes in congenital syphilis, general paralysis of the insane, and the "tabes-psychoses." The last hundred pages of the volume deal with trypanosomiasis, disseminated sclerosis, and diffuse sclerosis (encephalitis periaxialis diffusa). The remaining disorders of the brain, including extrapyramidal conditions, are to be considered in the forthcoming second part.

The relationship of anatomical changes to clinical features is not overlooked, nor the necessity for suspending judgment on many points, where, however, the conflicting views are presented and summed up with great lucidity; this is done, for example, in a masterly way in the "observations on the pathogenesis of general paralysis."

The references to literature are full, and the photomicrographs numerous and clear.

Ueber einige neuere diagnostische und therapeutische Verfahren in der Neurologie. Von E. VON THURZO. S. 78. Berlin: S. Karger.

A series of addresses, mainly on diagnostic and therapeutic problems, which the author has given before different societies are brought together in this small volume. The more important are those on the abduction reflex of the toes, on the introduction of air by the lumbar and suboccipital routes for the purpose of encephalography, and on the modification of the Lange reaction introduced by Sicard and Haguenan.

The article on the influence of malarial infection in the early stages of syphilis on the subsequent development of neurosyphilis brings out some interesting points. Apparently the infection does not make the occurrence of nervous symptoms less likely, but when either tabes or dementia paralytica develops it runs a more favourable course.

The Pathology of the Eye. By JONAS FRIEDENWALD, A.M., M.D., F.A.C.S. Pp. 346, with 253 illustrations. London: Henry Kimpton. Price 21s. net.

In this book an attempt is made to link the pathology of the eye to that of the other tissues of the body. This attempt is only partially successful, for one cannot expect tissues so specialized and delicate as those of the eye to react in the same way to bacterial and metabolic poisons as less highly differentiated tissues. In this way the problems of eye pathology are similar to that of neuropathology, but while the eye is more limited in size it contains a greater variety of special tissues than the brain. Several of these, such as the cornea, the lens and the vitreous, are avascular and are therefore more vulnerable than any vascularized tissues. The author has indeed, as far as knowledge goes, given a very clear picture of ocular pathology, linking it with general pathology on the one hand and with what can be seen during life on the other hand. He is disinclined to discuss theories of causation unless these are well established, and prefers a confession of ignorance or of philosophic doubt to a presentation of the theories which have at one time or another been put forward to explain phenomena. While this attitude saves space, it is in some respects disappointing to the neurologist, especially in relation to the causation of papillœdema and optic neuritis and atrophy. The various problems related to glaucoma are rather more fully discussed, but the work of Duke Elder on the circulation of the intra-ocular fluids is scarcely mentioned. The parallelism between this circulation and that of the cerebrospinal fluid is close that the author might have benefited by a study of the recent work on the latter subject. The book is richly illustrated with photomicrographs, most of which are excellent.

The Meaning of Sacrifice. By R. MONEY-KYRLE. (International Psycho-Analytical Library, No. 16.) Pp. 273. London: Hogarth Press and Institute of Psycho-analysis. 1930. Price 18s.

Since the publication of Freud's "Totem and Tabu" a number of writers have applied psycho-analytic theories to the study of anthropology. Dr. Money-Kyrle has here collected from standard works the available data about rites of sacrifice and attempted to elucidate their meaning, expressed in terms of unconscious impulses. To these unconscious impulses, as conceived by the Freudian School, and particularly to the significance and consequences of the Œdipus situation, he devotes the first part of the book. It is impossible to examine his conclusions and methods in a brief notice. The book is lucid and well-informed, less dogmatic than some similar works, and can be recommended to the attention of all who are interested in the interpretation of primitive customs.

Geschehnis und Erlebnis. Zugleich eine historiologische Deutung des psychischen Traumas und der Rentenneurose Von ERWIN STRAUS. S. 129. Berlin: Springer. 1930. Price Rm. 6.60.

This little book represents an admirable attempt to clear up fog. Among nebulous terms, "psychic trauma" is one of the commonest used in psychiatry; Dr. Straus clarifies it on grounds of theoretical psychology and empirical observation of cases, using the familiar picture of compensation-neurosis as the means to this end. Time-relationships, with which he has concerned himself in an earlier paper, are regarded as the central problem around which are grouped related matters, such as the author's concept of "Deformation" as a fundamental feature in the psychopathology of neuroses and perversions.

The book is critical, close-woven and predominantly psychological.

Lebensschicksal und Persönlichkeit ehemaliger Fürsorgezöglinge. Von ADELHEID FUCHS-KAMP. S. 172. Berlin: J. Springer. 1929. Price M. 18.60.

This sociological study is the latest of the series of Heidelberg monographs on criminal psychology, in which, among others, Kurt Schneider's study of prostitutes and Homburger's of the criminal insane have appeared. The histories of sixty-five former inmates of the Flehingen Reformatory in Baden have been compiled from institution and Court records, letters, &c., and an examination of their present personality and social relations carried out with as much completeness as possible. From the data thus obtained interesting conclusions are drawn as to the relation of criminality to psychopathic disposition. The authoress makes no reference to the thorough and more extensive studies of this kind that have been made in the United States.

Handbuch der Geisteskrankheiten. Herausgegeben von OSWALD BUMKE. 2ter Band, allgemeiner Teil 2. Störungen des Wollens, Handelns, Sprechens. S. 377. Berlin: J. Springer. 1928. Price Rm. 37.70.

This volume covers the difficult field of disorders of speech and conduct. Professor Bostroem writes in the opening section a concise account of the psychology and pathology of the will; he emphasises, however, that any isolated consideration of the phenomena of will represents an abstraction.

K. Birnbaum is responsible for the section dealing with the psycho-reactive symptom formations. The difficulties in the way of delimiting such a group are discussed, and the general description—"psychopathological phenomena which appear as pathologically conditioned reactions to psychic stimuli"—is expanded with the lucidity and grasp one expects of this author.

Catatonic disorders are discussed in detail by Bostroem, who also deals with syndromes dependent on lesions of the basal ganglia.

A monograph of 120 pages on "Aphasia, Apraxia, Agnosia," by Thiele, of Berlin, concludes the volume. Considering the enormous literature on the subject and its peculiar difficulties one welcomes a careful review as this of the development and present state of opinion; the author has wisely contented himself with description and appraisal, a sufficiently onerous task, and the result is a well-proportioned compendium which will be of the utmost value to anyone concerned with the problem of aphasia and allied disorders.

Lehrbuch der Geisteskrankheiten. Von OSWALD BUMKE. Dritte Auflage. S. 806 mit 160 Abbildungen. München: Bergmann. 1929.

This well-known textbook by the Professor of Psychiatry in Munich has been cut down to a handy size and otherwise revised for the purposes of a third edition. Conservative and critical, it is a sound exposition of psychiatric teaching, embodying much personal experience and the results of research in Germany so far as the latter has been kept free from any tincture of the Freudian doctrine, with which Professor Bumke will hold no terms. It is a pity that the sections on treatment are relatively so brief; it is a sign of honesty, no doubt, but more discouraging than the present state of affairs would warrant, especially in the case of schizophrenia.

Manuel élémentaire de Psychiatrie. Par M. NATHAN. Pp. 319. Paris: Masson. 1930. Price 30 francs.

This little book is so unpretentious in its title that one can hardly find fault with its defects of omission, but there are other faults, of arrangement and nosology, which spring from good intentions, but are especially unsuited to an elementary manual. The author applies the modern views about syndromes and dynamic types of reaction with such zeal that the overlapping between his "psychoses" and his "psychiatric syndromes" is bewildering, while for the beginner the lack of any introductory sections on general psychopathology and symptomatology is another stumbling-block. Little attention is devoted to the work of any but French psychiatrists.

Insomnia. By H. CRICHTON-MILLER. Op. 172. London: Arnold and Co. 1930. Price 10s. 6d.

Its sub-title, "An Outline for the Practitioner," describes the scope of this book. Several pages are devoted to the nature of sleep and to its physical and mental concomitants, but owing to the absence of a critical survey of the numerous theories presented, the reader not familiar with recent investigations on the subject is in danger of being confused.

The psychological aspect of sleep and the psycho-therapeutical treatment of insomnia claim most attention, but the uses of physical and medicinal treatment are adequately considered.

La Folie et la Guerre de 1914-1918. A. Rodiet et A. Fribourg-Blanc. With 10 plates. Pp. 187. Paris: Félix Alcan. 1930. Price 30 francs.

Although this monograph concerns the cases of mental disorder met with in the ex-Service man of France, it is actually a textbook of psychiatry in itself and covers the whole ground of mental disorder. The authors come to the same conclusion as have English observers in the same field, that is, that while the war has coloured the form and substance of the psychopathic states, the conditions themselves were clinically exactly like those in civil practice, and, in addition, that the war has not brought into being a new form of mental disorder. What the war has certainly brought out, in the view of the authors, has been the germination of constitutional and hereditary peculiarities until these became, in the stress of warfare and its call upon the instincts, fully-fledged psychopathic states. As regards alcoholism, they again corroborate the views of English observers that the drug itself was not the cause of the disorders arising, but that the alcohol acted upon excitable tissue because of the circumstances of war and the constitution of the subject, producing chronic mental disorder long after the effects of the alcohol had worn off. One unusual feature of this volume is the really artistic plates, many of them excellent drawings of cases of mental disorder. The photographs, too, of schizophrenic attitudes are quite unique.

Körperbau und Geisteskrankheit. By Max Schmidt. Pp. 206. Berlin: Julius Springer. Price 16 marks.

The investigations of Kretschmer into the relationship of physique to mental reaction type has led to as rich a crop of investigations as any discovery in the last forty years of psychiatry, with the exclusion, perhaps, of Freud and his school. This work has been almost entirely confined to Germany, and this volume is another example of the extraordinary painstaking way of the German psychiatrists, and also, let it be added, of the public support that is given to the publication of these magnificent monographs. The monograph is a frankly statistical clinical study of the two great physical types, the pyknic associated with the cyclothymic disposition, and the asthenic (leptosome) physique associated with the schizothymic disposition. Only students of psychopathology who have a first-hand knowledge of this specialized department will be able to read this volume critically, but all psychiatrists should make themselves acquainted with what is a very important and striking contribution to the psychophysics of mental disorder.

The study of morphology alone is not likely to solve the problems of reaction type, but viewed in the light of ethnology on the one hand and metabolism on the other, these studies in morphology, or "Korperbau," may prove to be important landmarks on the psycho-pathological road. Those who are doing work of this character will be very grateful to the authors for their thorough and painstaking researches.

Psychiatrie du Médecin-Praticien. By M. DIDE et P. GIRAUD. Second edition. Pp. 453. Paris: Masson et Cie. 1929. Price 45 francs.

This textbook on psychiatry is constructed on very formal lines, and, on the whole, is not controversial in matter, although the authors do not take up a modern psychological point of view; that is to say, they are almost untouched by Freud, and in their consideration of the large group schizophrenia, they are inclined to differ rather strongly from Bleuler. There is, as is so commonly found in French textbooks, a somewhat bewildering subdivision of subjects This is perhaps the result of what is undoubtedly the French genius for stylistic descriptions of symptoms and behaviour.

The book is very beautifully illustrated with photographs of persons in typical attitudes of mental disorder; some of them are certainly the best we have seen published in psychiatric textbooks. These pictures, in a way, are the keynote to the author's attitude. Although a book of only 450 smallish pages, there is an enormous amount of material, and for students especially engaged in this branch of medicine they will be sure to find many new clinical facts.

Innere Sekretion und psychische Prozesse. By W. N. SPERANSKI. Pp. 150. Berlin: S. KARGER. 1929. Price M. 8.

Dr. Speranski's monograph is a systematic attempt to organize our present knowledge of endocrinology and its relation to psychology. As a member of the Russian school, he naturally opens his thesis with a discussion of Hormono-reflexology, i.e., he relates the activity of the hormones to the total activity of the organism considered behaviouristically. The James-Lange theory of the emotions comes under examination in this connection.

The burden of the monograph rests mainly upon a physiological and somewhat philosophical discussion of the neuropathology of hysteria and katatonia. The subject that Dr. Speranski has chosen is one of the first importance to all students of neurology who are struck by the common mechanisms that seem to be underlying such clinical conditions as hysteria, catatonia, mutism rigidity and katalepsy.

To have attempted further to relate such neurologically functional states to the internal secretion is an heroic effort. The author has not succeeded on the clinical level, but he has made a contribution to the general problem. His thesis, however, illustrates the danger of interpreting all behaviour in terms of neural mechanisms that are still highly speculative. All attempts to subsume the bewildering variety of psychic phenomena under simple natural concepts are in danger of losing those physiological events which alone give meaning to psychopathological states.

Le Développement mental et l'Intelligence. Par HENRI PIÉRON. Pp. 95. Paris: Felix Alcan. 1929. Price 10 francs.

With his characteristic gift of perfect condensation, Professor Piéron has put into these four lectures all the current matter relative to mental testing as a measure of intelligence and its development.

In the first lecture on stages of mental development, the author indicates very emphatically the importance of correlating successive stages of mental maturing with physical maturing. He also stresses the importance of realizing the fact that socialization is a measure of full linguistic development.

Lecture II concerns the history and method of mental testing. Than this chapter of twenty pages we have never seen a more masterly survey of what is an immense literature. Most interesting lecture of all, particularly to the clinical psychologist, is that which discusses mental levels with their relation to "mental profiles."

No practical picture of a mind can be of clinical value unless it presents the differential endowment of a subject. The illustration cases of profiles at different mental ages are of great value. The last lecture is methodological and gathers up all the data of the preceding lectures in a plea for analytic evaluation of data. A small book by a master hand.

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of "Brain." If reprints are required in pamphlet form, with wrapper, title-page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BALE, SONS & DANIELSSON, Ltd., 83-91, Great Titchfield Street, London, W.

Members of the Neurological Section of the Royal Society of Medicine can obtain the Index of "Brain" for the Volumes I to XXIII inclusive, that is, from its commencement to the end of 1900, from Messrs. MACMILLAN & CO., Ltd., St. Martin's Street, London, W.C., at the price of 6s. 6d., post free.

To those who are not members of the Neurological Section of the Royal Society of Medicine the price is 8s. 6d. net, and the volume may be obtained through any bookseller.

EDITOR.

OCTOBER, 1930.

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BRAIN.

PART 3, VOL. 53.

THE POINTING POSITION OF THE HAND AS A PATHOLOGICAL AND PRIMITIVE REFLEX.[1]

BY PROFESSOR A. A. GRUNBAUM.

(*From the Psychiatric-Neurological Hospital of the University of Utrecht.*)

OUR symbolic expressive movements may be divided into two distinct groups. To one of them belong gestures which clearly show their origin in primitive biological behaviour. Thus the movement of threatening with the clenched fist is nothing but the beginning of an attack. If the affect increases, the threatening with the fist may change into a blow against the adversary.

In contrast with these gestures, representing the beginning or the decrease of a purposive movement, are others, no less frequent, the relation of which to some biological situation is not clear. Why, for example, has the military salute the well-known form of elevating the extended right hand to the forehead? Have we to do here with mere convention founded on tradition, or is this gesture based upon biological or physiological mechanisms which are preferred to other motor complexes in the given psychical situation? Though we may believe those gestures which we use as a kind of colloquial language to have at least a local social historical cause, yet in most cases we are unable to trace the biological origin of such symbols.

In the following pages I will try, starting from some ontogenetic and pathological observations and experiments, to explain how it is that when indicating some object we do so with the characteristic position of pointing: right arm fully extended, the back of the stretched hand upwards with the index extended and the other fingers flexed towards the palm, either clenched to a fist, or hanging inactive. I was led to this problem by the observation that the characteristic position of pointing, which we make as a voluntary movement, which is excited automatically as a synergy, or which is seen in various extrapyramidal lesions as a spasm (see below), may also be induced by a definite method as a reflex.

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[1] By the kindness of Prof. Kurt Goldstein, I have had an opportunity since this manuscript was finished of seeing the proof-sheets of a paper of his pupil, Hans Cohn (Weitere Beobachtungen über Haltungs und Bewegungsstörungen bei Schadigung des Stammganglien-apparates." "Zeigestellung," Mitbewegungen, "induzierte Tonuserscheinungen," already published in *Zeitschrift für die gesamte Neurologie und Psychiatrie*, Bd. 125, H. 2/3, S. 327.) This paper also mentions the provocation of the "pointing position," but does not discuss the reflex character of the phenomenon.

This observation was first established in the following case:—

F. H., a boy aged 10. He was said to have "trembled" from birth, and to have sudden transient accesses of pallor at the age of 8. He appeared to be imbecile, and had never walked or talked normally. There was temporal pallor of the optic discs. The pupils were unequal and immobile. Corneal and conjunctival reflexes were absent. Visual acuity seemed to be normal. Articulation was defective and the protruded tongue was restless. There were jerking movements of the head and limbs, variable muscle tone and increased tendon-jerks. Co-ordination was defective with intention tremor and ataxy. The right plantar response was extensor, the left was not obtained. Sensation appeared normal.

The pointing position of the hand was best elicited with the patient propped up in bed, the arm flexed and pronated and supported on a pillow, and the fingers almost fully extended. The patient was told to shut his eyes, and the endeavour was made to divert his attention from the procedure to be described. The index finger was then stretched by the observer. Thereupon the remaining digits actively flexed, the middle finger least, the little finger most. On releasing the stretched index, the pointing position of the hand was maintained for a brief interval. Other passive movements of the index evoked a similar response; as rotation of the index on its long axis. Moderate degrees of passive lateral deviation of the index (ulnarwards or radialwards) evoked a less active response than stretching (fig. 1).

The converse reaction, namely, active extension of the index when the remaining digits are passively flexed on the palm, did not occur. Pin-prick, pressure, thermal and electrical stimuli applied to the extended index did not elicit the "pointing position" response, i.e., active flexion of the remaining digits.

Thus the characteristic pointing position of the hand was elicitable only by deep sensory stimuli arising in the neighbourhood of the joints of the index finger, comparable stimuli to the other digits being without effect.

The phenomena thus described were observed in the right hand, but a less ample and slower response of the same nature was also obtained from the left hand. In both cases undue frequency of stimulation led to fatigue of the response, more readily in the left than in the right hand.

Under favourable conditions, as after rest, it was often observed that if the pointing position were provoked on the right side, the same position simultaneously, though less obviously, appeared in the contralateral hand (fig. 2). Scarcely any movement of the index in its distal joint was to be seen, but a distinct flexion of the other fingers could be observed, the thumb going into a flexion-adduction position. I did not succeed in exciting the crossed phenomenon on the right side from the

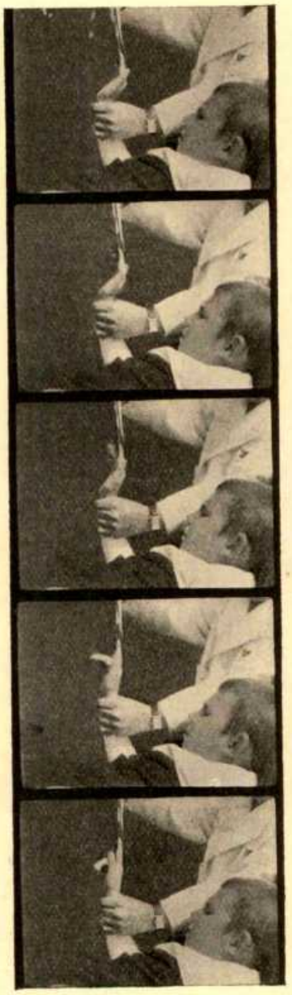

FIG. 1.—Passive extension of the index induces a "pointing position" of the hand; the three ulnar fingers and the thumb assume flexed positions while the index remains in active extension.

left hand. The contralateral "pointing position" fatigues even more rapidly than the ipsilateral phenomenon, and after three or four repetitions the mechanism is exhausted, recovering relatively early from fatigue. When the patient's arm was held passively in a flexed position for a longer time, slow movements of the fingers set in, which resembled the athetotic movements described by O. Förster [3]: "slow alternating movements of flexion and extension of the fingers" [1].

These movements might perhaps be interpreted as voluntary movements of the fingers resulting from an uncomfortable position of the arm. The regularity of their rhythm, the stereotyped positions assumed, and their regular production by passive movement of the index indicate involuntary activities.

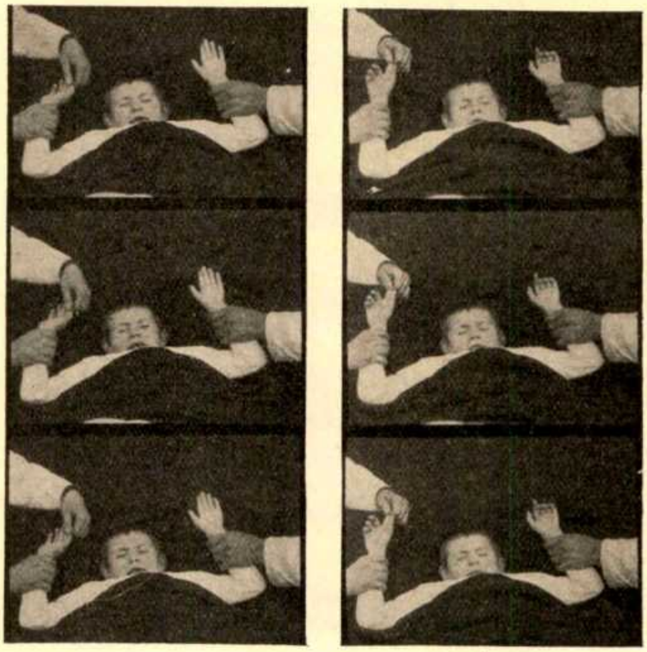

FIG. 2.—The beginning (a) and the end (b) of a series of photographs which show the appearance of the "pointing position" in the opposite hand.

We have first to decide whether we are dealing with a reflex or not. A similar question has been raised by Carl Mayer [12], especially in relation to the finger, "Grundgelenk-Phänomen," that has since become an accepted aid in the diagnosis of lesions of the pyramidal system above the level of the cervical cord [5].

We need not consider, in discussing the "pointing position," the objection that the "Grundgelenk-Phänomen" is not a reflex, but a conscious pain reaction (A. Meyer), for the adequate stimulus of the "pointing position" does not excite pain, while painful stimuli do not elicit it. Nor can it be due to a mechanical effect without participation of the centrally excited muscular contractions, for in normal adults even a violent passive stretching of the index does not excite bending of the other fingers. Moreover, the fact that we can provoke the pointing position contralaterally shows it does not depend merely on mechanical relations.

That it is not a purely voluntary movement is proved by the fact that in our case the phenomenon was always more distinct on one side of the body than on the other, and that after a short series of succeeding reactions fatigue ensues, disappearing quickly after resting he hand.

Nor is the pointing position a result of a withdrawal movement or something of that order, for painful and thermal stimuli provoking withdrawal do not excite it. Further, stimuli which excite the pointing position at the index remain without any effect when applied to the other fingers.

The selective stimulus necessary to evoke the pointing position as well as the contralateral response, the exclusion of a voluntary element and of mechanical factors, all indicate the reflex character of the pointing position. We may therefore call it the "pointing reflex." It is a co-ordinated multi-muscular reflex, in which by a specific stimulus coming from a certain region (index) of a functionally connected group of muscles (fingers of the hand) simultaneous movements are excited. It leads to a position (pointing position) which can also be assumed as a voluntary purposive reaction.

In order to determine its reaction time, the reflex was cinematographically recorded, the film being moved with constant velocity (sixteen pictures per second). The stimulus was the application of a forceps to the index; this was easily visible on the film, and the number of the pictures between the closing of the forceps and the first visible change of position of the ulnar fingers relative to a fixed point therefore gives approximatively the latent time of the reflex.

This interval averaged between three to five pictures, so the latent time is about 0·25 second. As the latent time of joint reflexes is 0·20 to 0·25 second, and of tendon reflexes, as the patellar, about 0·05 second [1], the reaction time of the pointing reflex belongs to the first class.

This points to also the reflex nature of the reaction, and suggests that it may be a reflex which can be influenced by cerebral mechanisms.

We must take into consideration here the co-existence of an "Eigen-reflex," as described by P. Hoffmann [7]. That the reaction is not a simple "Eigen-reflex," is shown by the fact that the latter is unilateral only, shows practically no fatigue, has a short reflex time and appears only as part of a "fremdreflectorisch" or voluntary movement. The pointing reflex has functionally a position intermediate between voluntary movements and the relatively fixed extrapyramidal motor disturbances, which also occasionally give rise to the typical pointing position.

It may be emphasized that, according to O. Förster [3], athetotic movements of the hand in the striate syndrome show a tendency towards flexion, ulnar adduction and pronation. The similarity of these movements to the position of the hand in pointing towards a distant object is obvious.

K. Goldstein and W. Bornstein [6] describe a case, probably with striatal disturbances, in which the right hand on becoming rigid assumed the pointing position, while after recovery from the spasm involuntary movements appeared, which produced the same characteristic position of the fingers. In another patient, aged 14, who suffered with epilepsy after injury of the head, the authors state that the pointing position occurred as a final tonic attitude during the epileptic fit [13].

A. Meyer [13] likewise observed the typical pointing position in a child with cerebral infantile paralysis of the right arm during the tonic phase of the epileptic fit. Similar cases reported by Pötzl, Schloffer and Lowenstein are cited by Meyer.

In a picture given by A. Jakob [9] we can see this pointing position of the hand in a somewhat exaggerated form as a contracture in a case of paralysis agitans.

I have observed this pointing position as a habit position ("Habitual-Stellung"), in several normal children between 2 and 4 years of age, especially when the arm had been stretched against gravity.

In the following case I was able to show, under certain conditions, an interesting transition between the pointing position as a reflex phenomenon and as a spontaneous habit position.

The patient was an epileptic, aged 20. His physique was infantile and poorly developed. His intelligence was that of a boy of 8 years, and there were epileptic changes in his character. Since childhood he had frequent fits without any aura, in which he fell to the left, his eyes turned to the right and his limbs were convulsed. His pupillary reflexes and vestibular reactions were normal. There were variations of muscle tonus in his arms and legs, athetotic-ataxic movements of his outstretched fingers, and Meyer's thumb phenomenon was more pronounced on the right than left. Ankle clonus could sometimes be obtained on both sides, but the plantar reflexes were indefinite.

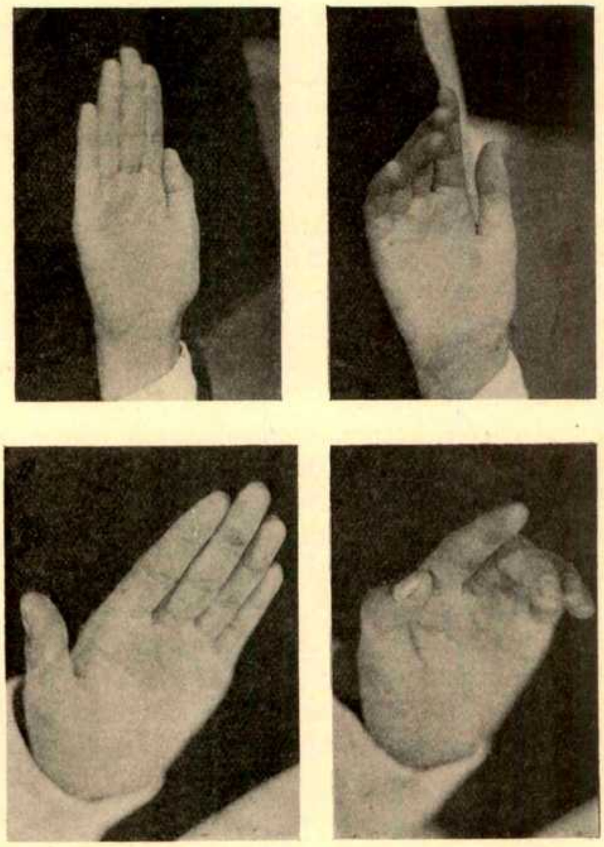

FIG. 3.—The "pointing position" appears in the one hand when the fingers of the other hand perform a series of active movements.

The pointing reflex could be obtained only when the tonus of the muscles was normal and the fingers relaxed. If the arm were moved about passively the muscles contracted tonically and the hand extended involuntarily; the pointing reflexes could not be then obtained. I found, however, that this tonic contraction could be prevented by active and passive movements of the opposite arm, and I could then obtain the pointing reflex.

The patient was seated and both arms were supported on a soft cushion. A screen was placed in front of one hand so that he could not see it. When made to open and close the hand he could see involuntary movements of the other hand occur, first flexion and extension of the little finger, then of the fourth finger, and finally all fingers flex at the metacarpophalangeal joints so as to approximate to the position of a closed fist.

When he tapped on a board a rhythm chosen by himself the fingers of the other hand assumed slowly the pointing position, the little finger flexed first, and then the fourth and third in succession, and the thumb became opposed. This occurred most readily when the arm was supinated.

If he voluntarily assumed the pointing position with either hand the fingers of the other hand passed into a similar position. This occurred whether the arm was pronated or supinated, but in the latter position the fingers flexed at their basal joints only, and the whole hand became more rigid than when the arm was pronated (fig. 3).

These observations show that voluntary movements of one hand in this patient excited movements and attitudes of the other hand which are similar to the pointing position. The movements excited in the resting hand tend to correspond to those in the moving limb. When the reaction is feeble the attitude tends to the pointing position, when strong to the grasping position.

This influencing of the tonus of one extremity by contralateral activity accords with observations I have described in which a provoked increase of the tonus of one arm causes a shifting of the tonus equilibrium from one side to the other, and disturbances of the innervation of the contralateral arm.

The pointing position can obviously be excited by motor mechanisms of different levels, and it therefore probably represents a functional unit. Goldstein and Bornstein [6] have come to the same conclusion from their investigations of analogous spasms, but the question whether there is a special " localization " of the pointing mechanism cannot be discussed here.

Further observation with children of different ages who already have a pointing synergy and are able to point to an object on demand, give the following results: If you ask them, e.g., " Show me the glass," when a glass is before them within reach, the first reaction is almost always a grasping and offering of the object. If we forbid the grasping of the object and tell the child to point only, we often see that he involuntarily begins a grasping movement. If the object lies beyond reach the child tends not merely to point to it, but to run to and grasp it and to bring the glass to the experimenter. Only when the child sees that it cannot reach the object it reacts to the question: " Where is that object?" by pointing. We can, however, provoke grasping instead of pointing under the following conditions: the experimenter arranges a number of objects before the child, so that it can grasp them, and gives his commands as: "Show me the glass," "Show me the apple," quickly in succession. If by this means we make the child perform a series of movements quickly, sometimes involuntary grasping instead of the movement of pointing appears. The pointing position of the hand appears where the act of grasping, which, it may be suggested, is biologically more primitive, is either suppressed or prevented by external conditions. I assume, therefore, that the pointing position is modified grasping, that it probably originated phylogenetically as an enfeebled and modified act of grasping in trying to reach an object which is beyond reach by extension of the fingers and arm. If you tell the child to grasp an object, as a lamp, which is hanging too high, he stretches his hand and all his fingers towards the object. Thus, the pointing position of the hand is an expression of the tendency to grasp under conditions where grasping is impossible. Pointing is partly an enfeebled grasping, partly a means of extending the grasping hand towards the unattainable object.

Considered as a symbolical expressive gesture, pointing is a sublimation of grasping. Phenomenologically, pointing towards an object has also some analogy with grasping it; by pointing towards the object it becomes virtually held.

The evolutional primacy of grasping over the act of pointing may be seen on comparing the muscular contractions and the relations of tonus in the grasping and the pointing positions of the hand. The tonus of the musculature and the degree of flexion of the fingers is greater in grasping than in pointing. The increase of flexion and of tonus during pointing occurs only when pointing energetically towards an object or towards a person. In affective states, as while disputing with somebody, we often point towards our opponent with the index extended and the thumb and the last three fingers closed to a fist. But if the dispute becomes more vigorous the index may flex and the hand assume a position as if grasping at the opponent.

It is interesting that in opening the fist gradually the tonus of the index first relaxes and it extends before the ulnar fingers.

The second, third and fourth fingers form together a closer synergic unit than does any of them with the index. The transition from grasping to pointing must, therefore, begin with the index. It is in advance of the other fingers in the change of position of the hand; while the other fingers are still tonically flexed it has begun to extend. Later, when the other fingers are still slightly flexed, the index is fully and tonically extended.

I regard these relations between the mechanisms of grasping and pointing as an example of a fundamental, functional correlation between all the characteristic movements and positions of the fingers. It may be looked upon biologically as a synergy, occurring very early in evolution and representing a purposive action, like grasping, climbing [2], the movements of rowing [4], &c.

It will be, however, more advantageous to study the development of these motor mechanisms in childhood than to indulge in biological speculations. By observations and experiments on newly-born and older children I found that the pointing position as a habit position and as a reflex movement develops from the original mechanism of grasping. It is well known that the hand of the new-born child generally assumes the fist position, with the thumb covered by the strongly flexed fingers. When the open hand is touched it closes reflexly immediately, the so-called grasping reflex; this is met also as forced grasping and groping in disease of the frontal lobes of the brain and in lesions of the basal ganglia [12], [15], [10], [8].

In newly-born children, who clearly showed the grasping reflex, I could not elicit a pointing reflex. The reason for this does not lie in any mechanical factor, as Trömner [16] states, but in the fact that the grasping synergy of the hand as a whole is still too strong.

The hand in new-born children only moves as a non-differentiated whole. If when the flexion tonus of the hand passes off for a moment, a pull is applied to the extended index, or to any other finger, all fingers flex again into a fist.

The pointing reflex is absent in the new-born child because the grasping reflex is still predominant, and because the tendency to stretching of separate fingers is not yet developed; this occurs only with the anatomical and functional development of the pyramidal system [2].

In normal children of about the age of 2 years, I could always demonstrate a pointing reflex. Up to the 5th or 6th year of age it is a normal phenomenon. The younger the children in whom the pointing reflex was elicited, the more frequently was it observed that reflex flexion of the fingers was excited not only by passive overstretching of the index but also by extension of the other fingers. The pointing position, as a reflex which can be produced only from the index, seems to develop from the grasping reflex. While the tendency to flexion predominates, it may still be excited by non-differentiated stimuli; then voluntary impulses begin to determine the pointing position as a whole. Later, when the pointing position appears as a habit position, only differentiated stimuli, as applications to the index, provoke the reflex flexion of the other fingers. Finally, these stimuli also lose their excitatory effect, and the physiological total process corresponding to the pointing position is seen only in the characteristic pointing position of the hand which it automatically assumes on voluntary initiation of the symbolical-expressive gesture of pointing.

It is noteworthy that the pointing reflex may be observed at the age at which also the "hand-arm phenomenon" of Leri and the finger-thumb reflex of Mayer appear, that is, according to Goldstein, only after the end of the second year [5]. The end of the second year is also the age at which the normal dorsiflexion reflex of the great toe changes into the normal plantar flexion reflex [11]. It is not yet clear how these coincidences are to be explained, but everything points towards the conclusion that particular mechanisms such as "grasping" and "pointing" form a unity, considered as physiological mechanisms and as modes of behaviour.

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CHRONIC PROGRESSIVE POLYNEURITIS, WITH REPORT OF A FATAL CASE.

BY HERBERT H. HYLAND
AND
W. RITCHIE RUSSELL.

(From the National Hospital, Queen Square, London.)

CASES of chronic polyneuritis may rarely progress so steadily and gradually as to give a clinical picture which superficially resembles that of progressive muscular atrophy. Remissions are the rule, but in the case here reported there was no period of improvement and death occurred about a year after the onset.

Sorgo [8] described a case of recurring polyneuritis in which the first attack of paralysis developed progressively during a period of five months.

Barnes [1] described cases as "toxic degeneration of the lower neurones simulating peripheral neuritis." His Case 1 is of special interest: a female, aged 21, in whom general loss of muscular power followed rheumatic fever and became progressively more extreme during a period of seven months. Bedsores and incontinence developed, with difficulty in swallowing and speaking; improvement then occurred.

Grinker [3] described a case of progressive polyneuritis in a painter, aged 65, who had suffered with colic. Progressive atrophy and paresis of the muscles caused death without remission in nine months. Autopsy revealed changes only in the peripheral nerves. There was no degeneration in the white columns of the cord. There was no shrinkage of the anterior horn cells and no change in the Nissl bodies.

Harris [4] considered that "slow chronic polyneuritis" was the most suitable term for describing this type of case. He reported two severe cases.

(1) A male, aged 31, whose symptoms came on following the appearance of large purpuric blotches on the legs. Some pain in the calves preceded a gradually progressive paralysis which increased in severity for twelve months. The arms were not affected until nine months after the onset. On examination seventeen months after the

onset, there was almost complete flaccid palsy of feet and legs, hands and wrists. All deep reflexes were lost and there was some anæsthesia in the periphery of all four limbs. No cause was found.

(2) The second case he reported was of a girl, aged 15, who became gradually weaker during twelve months until all four limbs were totally paralysed: she was unable to raise her head from the pillow and her facial and masticatory muscles were weak. Apart from slight paræsthesiæ at the commencement, there were no sensory symptoms. No improvement occurred until eighteen months after the onset, when she slowly began to regain power and recovered completely in another two years. In this case also no cause was found.

The case which is the subject of the present study was admitted to the National Hospital for Nervous Diseases on October 10, 1929, under Dr. James Collier.

Mrs. C., aged 45. She complained of paralysis of the arms and legs, breathlessness and spasms of choking. She was hardly able to speak owing to respiratory embarrassment, so the history was mainly obtained from her husband.

Previously she had enjoyed particularly good health. No other illness was known. She had been married for seventeen years. There had been two miscarriages but no children.

Her father died of "old age" at 76. Her mother died in a mental hospital aged 55. Eight siblings were alive and well; none have died.

As to habits, she only rarely takes alcohol, has always a good appetite and takes a varied diet. No contact with any possible poison was discovered.

History of illness.—A year ago she began to complain that everything was too much for her and that she readily became exhausted. About the same time she had a rash over the left side of her face and neck. This began on her neck and spread gradually in the course of six weeks over the side of her face. It then gradually receded, disappearing first from the forehead and last from the neck. There was no temperature or marked malaise; no crusts or oozing. The eye was not inflamed and no scar was left. There was severe local irritation which kept her awake at night.

Ten months ago she would complain that her arms felt weak when washing. Thereafter the muscular weakness became progressively worse. Her knees "gave way" five months ago and since then she has been unable to walk. Her arms also became worse and she was admitted to Redhill Hospital (Edgware) on June 12, 1929 (four months ago), where she remained till August 6, 1929.

NOTES FROM REDHILL HOSPITAL RECORDS.

There was no temperature. The fundi were normal. The pupils were equal and reacted normally. Slight nystagmus was present on looking to the right. Marked hippus was present. The patient was unable to stand owing to great weakness of the legs. The upper extremities were almost powerless. No contraction of the biceps or pectoralis major could be demonstrated on either side. She was able to move the fingers a little in both hands. Some wasting of the interossei was present.

The faradic responses were normal in the muscles of the arms and legs. All deep reflexes were absent. There was no loss of sensation. The lower limbs were hypersensitive to pressure.

The fractional test meal and blood-picture were normal. No stippling of red-cells was seen.

The Wassermann reaction was negative in the blood and cerebro-spinal fluid. The latter contained one cell per c.mm.

She was seen by Dr. Russell Brain on July 23, 1929, who diagnosed her condition as a toxic polyneuritis.

While in Redhill Hospital she continued to become weaker and her husband took her home, where the downward progress continued steadily. There was no apparent period of improvement throughout her illness. She became completely powerless in her limbs and during the last two months of her life had numerous choking attacks which became more and more frequent. She developed great respiratory distress during these and became very blue. She also had difficulty in swallowing.

Patient stated that when the weakness of the hands commenced it was associated with feelings of "pins and needles," and numbness in both hands.

Clinical examination on admission to the National Hospital, Queen Square.—The patient sits propped up in bed. Her breathing is laboured and her face cyanosed. The respiratory rate is 32 per minute, the pulse rate 110 per minute and the temperature 99° F. She has frequent spasms of silent coughing during which she becomes greatly distressed. The expulsion of some mucus from the larynx is followed by some relief. Speech is clear but difficult owing to breathlessness.

Cranial nerves.—Visual acuity is good. The discs and retinæ are healthy. The pupils are equal, central, circular and regular in outline. They react briskly to both direct and consensual light, and on accommodation. The external ocular movements are full. There is fine horizontal nystagmus on looking both to right and left, the quick component being in the direction of gaze.

The corneal reflexes are brisk and equal. No sensory loss to pin prick over the face was discovered. There is no facial weakness or palatal palsy. The sterno-mastoids act with respiration, but are weak. The trapezii are very weak. The tongue is protruded straight and shows no atrophy or tremor.

Motor functions.—The patient is utterly helpless. The upper and lower extremities are flaccid and motionless. The only movement possible is in the fingers of the right hand, and this is very slight. All the muscles are somewhat atrophied and this is particularly apparent in the small muscles of the hands.

The muscles of the trunk and neck are also largely paralysed. Her neck unless supported falls forward. With each inspiration the head moves forward with the contraction of the sterno-mastoids. No fibrillation was observed.

Reflexes.—The biceps, triceps, supinator, knee and ankle jerks are all quite absent. The plantar responses are both flexor. There was no incontinence of urine or fæces while in hospital.

Sensory functions.—Sensibility to pin-prick was tested without eliciting any peripheral or other loss. Pressure on the calf and hand muscles causes great pain. The soles of the feet are very sensitive.

No trophic changes are apparent.

Examination of the heart shows no abnormality. Numerous moist râles are heard all over both lungs.

Progress.—Her breathing became more and more embarrassed. Abundant frothy expectoration was brought up with great difficulty and exhaustion. She died two days after admission, on October 13, 1929.

POST-MORTEM EXAMINATION BY DR. GREENFIELD TWENTY-FOUR HOURS AFTER DEATH.

The body was well-nourished but some wasting of the fore-arms was evident. The small muscles of the hands were soft but not obviously atrophic.

The brain and spinal cord were removed. The brain was quite normal in appearance. The cord in the upper dorsal region appeared rather softened. The anterior and to a less extent the posterior roots of both the cervical and lumbar enlargements were greyish but not atrophied.

The nerves in the arms were definitely larger than normal throughout their extent from the brachial plexus downwards and were pinkish in colour. The sciatic nerve was also pinkish but was rather smaller than normal, though possibly more rounded in shape. Pieces of the ulnar, median, sciatic, musculo-spiral, internal cutaneous nerves and brachial plexus were taken for further examination.

Several of the dorsal root ganglia from the cervical, thoracic and lumbar regions were removed with the cord. Pieces of the biceps brachialis, biceps femoris, erector spinæ and diaphragm were kept for examination.

Thorax and abdomen.—The *right lung* was partially collapsed in its lower lobe, so that fairly large pieces sank in water. Apart from evidence of early broncho-pneumonia in the collapsed areas the lungs elsewhere appeared healthy. Microscopic examination of the right lower lobe revealed a large area of collapse surrounded by extensive broncho-pneumonia and much œdema.

The *heart* showed nothing abnormal macroscopically. The *thymus* macroscopically was definite. It was firm and pinkish in colour. Microscopically a large amount of thymic tissue remained but nothing abnormal was recognized.

In the *liver*, macroscopically, nothing abnormal was noted. Microscopically a considerable amount of congestion was present and some fatty change throughout the lobules. A little cellular proliferation was evident around the portal spaces. There was no evidence of cirrhosis.

The *spleen* macroscopically was normal apart from evidence of mild venous congestion. The *kidneys*, macroscopically, showed only some passive congestion. Microscopically no other abnormality was noted.

The *suprarenals* were merely thin-walled empty capsules.

EXAMINATION OF THE NERVOUS SYSTEM AND MUSCLES.

PERIPHERAL NERVES.—Technique: After ten days' fixation in 10 per cent. formalin, pieces of the median, ulnar, musculospiral, sciatic, internal cutaneous nerves and brachial plexus were imbedded in celloidin. Sections of these nerves were also cut on the freezing microtome. Longitudinal and transverse sections were stained with hæmatoxylin and van Gieson, hæmatoxylin and eosin, Scharlach R., toluidin blue and by the Weigert-Pal method.

Microscopic findings.—On examination the nerves all showed the same changes, differing only in degree. Longitudinal sections of the median, ulnar, musculospiral, sciatic and brachial plexus revealed extensive areas of myelin degeneration. The myelin was seen to be beaded and irregular in many places and occasionally it lay between the nerve-fibres in "balls." It was not infrequently absent or almost absent over quite large areas.

Transverse sections of these nerves stained to show myelin illustrated even more strikingly the amount of degeneration. In the median nerve, which was the most severely affected, the majority of the axis cylinders were entirely deprived of myelin and many of the remainder had an abnormally small amount. The funiculi, however, were not all affected equally; some had comparatively little myelin loss, whereas in others scarcely any myelin sheaths remained. The outer cord of the brachial plexus showed almost as advanced a degree of myelin degeneration as the median nerve. The posterior cord of the plexus, the ulnar and musculospiral nerves were less severely affected and the large majority of axis cylinders in these nerves were surrounded by a myelin sheath; in many instances, however, the sheath consisted of an irregular and frequently incomplete ring. In the sciatic nerve also a large proportion of the fibres were deprived of myelin or possessed an inadequate amount. This nerve also demonstrated well that the brunt of the degenerative process tended to fall on certain bundles, leaving others relatively little damaged. (Figs. 1 and 2.)

The internal cutaneous nerve was the only purely sensory nerve examined. In it the myelin degeneration was considerable but much less than in the motor and mixed nerves.

The other changes observed in the nerves were roughly proportional in degree to the amount of myelin loss present. They consisted of a moderate increase in the connective tissue between the nerve fibres, but this was not sufficient to account for the increase in size of the nerves noted at post-mortem examination. Proliferation of the sheath of Schwann cells was a conspicuous feature in all the nerves, and the nuclei were, in general, larger and more circular in shape than is normally the case.

PLATE XI.

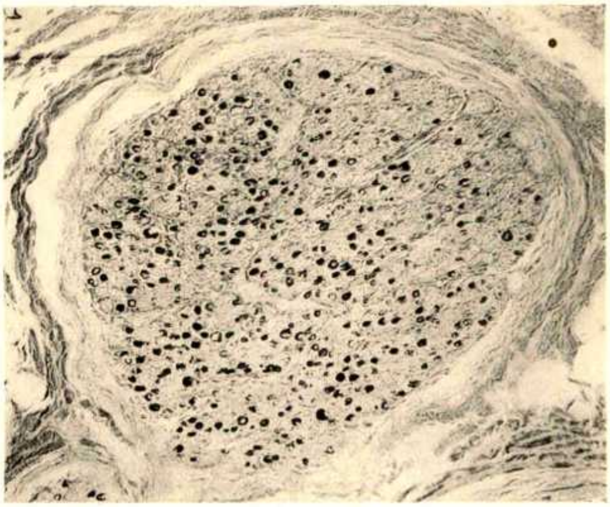

FIG. 1.—Sciatic nerve—high power. Shows advanced demyelination in a nerve bundle. Weigert-Pal (celloidin section).

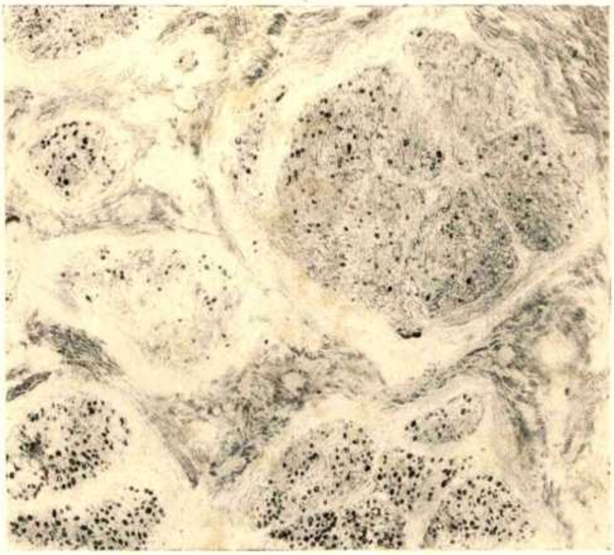

FIG. 2.—Median nerve—low power. Shows severe myelin loss, much more pronounced in some funiculi than in others. Weigert-Pal (celloidin section).

To illustrate paper by Herbert H. Hyland and W. Ritchie Russell.

PLATE XII.

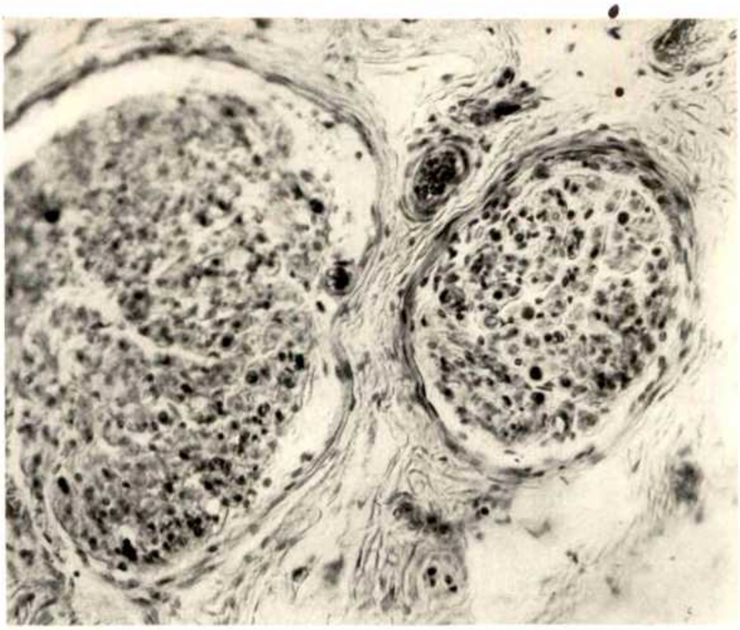

FIG. 3.—Two intramuscular nerves in the biceps femoris — high power. Myelin degeneration is advanced. The dilated perineural space is seen in both nerves, but is more prominent in the larger. Weigert-Pal (celloidin section).

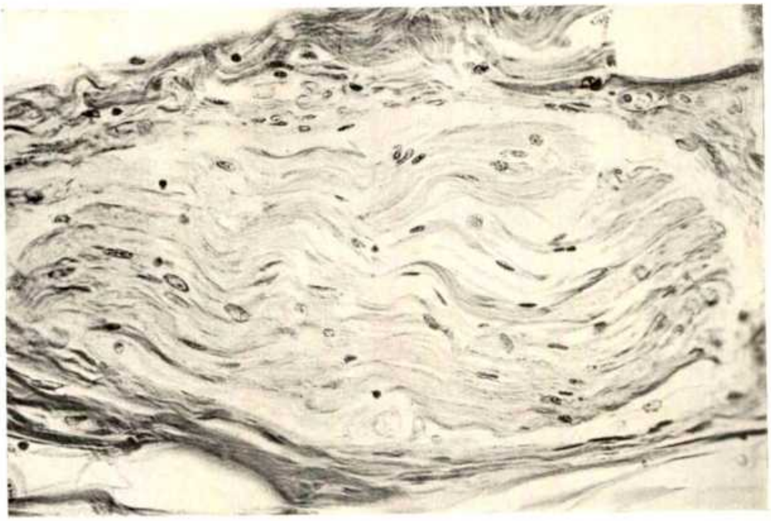

FIG. 4.—Small nerve in the biceps brachialis—high power. The dilated perineural lymph space is well seen. The fibres are seen to be separated from each other, suggesting œdema within the nerve. Hæmatoxylin and van Gieson (celloidin section).

To illustrate paper by Herbert H. Hyland and W. Ritchie Russell.

PLATE XIII.

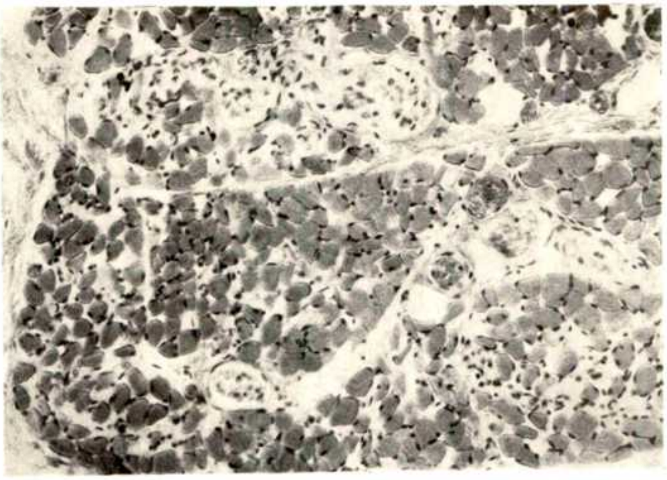

FIG. 5.

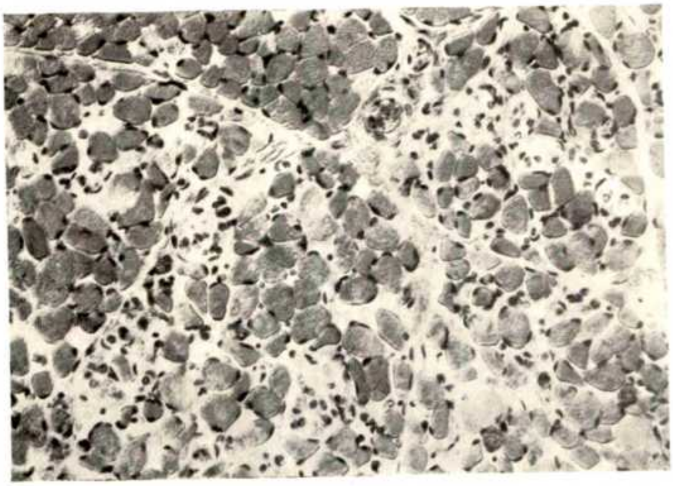

FIG. 6.

FIGS. 5 and 6. — Biceps brachialis showing many small nerves grouped amongst atrophied muscle fibres. × 100. The nerves appear to be very cellular owing to the presence of endothelial cells in the nerve bundles. Around some of the nerves dilated perineural lymphatic spaces are evident. Hæmatoxylin and van Gieson (celloidin section).

To illustrate paper by Herbert H. Hyland and W. Ritchie Russell.

PLATE XIV.

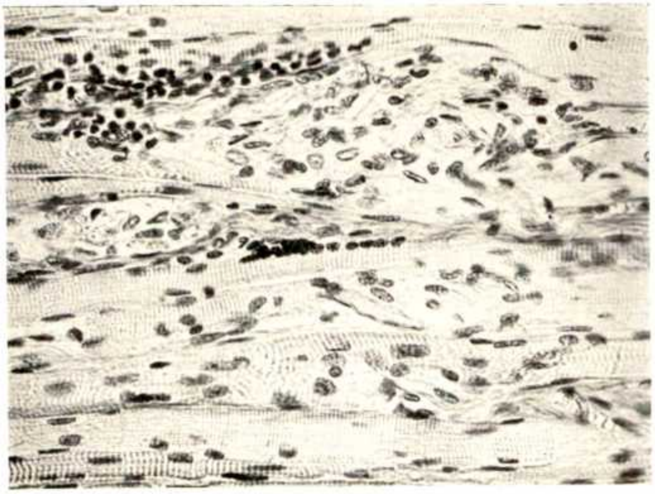

FIG. 7.—Small nerves in longitudinal section of biceps brachialis. × 200. Shows endothelial cells among the nerve fibres and infiltration with small mononuclear cells adjacent to the nerve. Hæmatoxylin and van Gieson (celloidin section).

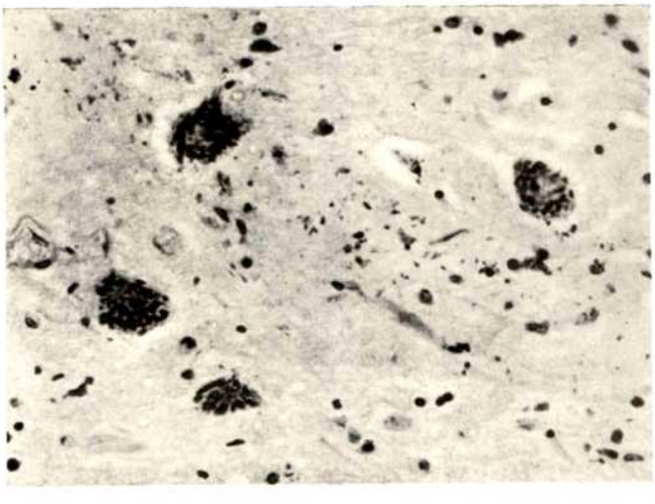

FIG. 8.—Eighth thoracic segment—high power. Four cells from the antero-mesial group of the anterior horn. Shows the roundness of the cells, the tendency to shrink and the variation in size of the Nissl granules, many of which are very large. The Nissl granules tend to be grouped more towards the centre of the cells, leaving a narrow, clear area at the periphery. The nuclei are central. Nissl (celloidin section).

To illustrate paper by Herbert H. Hyland and W. Ritchie Russell.

In addition to the proliferative changes there was an extensive infiltration by mononuclear cells throughout the nerves. Most of these cells were small lymphocytes, but a number of endothelial wandering cells was present and also a few plasma cells. No polymorphonuclear cells were seen. The infiltration was principally between the nerve bundles in the connective tissue spaces, tending to be more dense in the vicinity of the blood-vessels; but in smaller degree it was scattered diffusely amongst the nerve-fibres as well.

The large clear nuclei of lymphoblasts were present around some of the blood-vessels, not infrequently forming several layers.

A great increase of vascularity was observed in all the nerves. No definite thickening of the vessel coats was present.

In sections stained with hæmatoxylin and eosin many cells were seen which at first glance resembled plasma cells. The cytoplasm, however, was slightly granular and was pink with a rose tint; is was also less extensive than in the plasma cell. The chromatin in the nuclei, although tending to have a peripheral distribution, was not so heavy as in the plasma cell. These cells were recognized to be tissue mast cells, and when stained with toluidin blue or methyl violet showed the characteristic granules.

In sections stained with toluidin blue the sheath of Schwann nuclei were seen, in many instances, to be surrounded by π granules.

Comparison was made between the nerves from this case and eleven nerves considered normal, to determine if the number and distribution of mast cells bore any relation to the pathological process present.

A number of π granules as great as that in the nerves under examination was present in nine of the normal nerves.

The number of mast cells in four of the normal nerves was considerably less than that found in the nerves of this case, but in five of the normal nerves it was just as great, and in the remaining two there were more mast cells to be seen than were present in any of the pathological nerves.

The mast cells in the normal nerves appeared to have a similar distribution to those in this case, lying for the most part amongst the connective tissue fibres and in the neighbourhood of blood-vessels.

It was concluded from this investigation that the number of π granules and mast cells in the nerves of this case were without pathological significance.

INTRAMUSCULAR NERVES.—Technique: After fixation for ten days in 10 per cent. formalin saline pieces of the biceps brachialis, biceps femoris, erector spinæ and diaphragm were embedded in celloidin and thin sections were cut and stained with hæmatoxylin and van Gieson, Mallory's aniline blue—orange G. stain and by the Weigert-Pal method.

Microscopic findings.—A striking change was seen in relation to the intramuscular nerves in all the muscles examined with the exception of the diaphragm. This was a dilatation of the perineural lymph spaces which appeared as clear zones surrounding the nerve bundles lined both internally and externally by connective tissue and in some places broken by fine strands of connective tissue (figs. 3 to 7). There was no definite evidence of serous or cellular exudate in these spaces. They were found around nerve bundles of all sizes, including the finest ramifications. The possibility that they might be due to artefact was considered, but was negatived by the regularity and constancy with which they appeared. A similar but very much slighter degree of the same change could be seen in the large peripheral nerves such as the median. It is likely here that the shrinkage of connective tissue fibres inseparable from formalin fixation would have reduced the size of the spaces and so rendered them less apparent.

In sections of these muscles there were areas where very small nerve bundles were numerous and closely grouped together. The nerves in these areas, both in longitudinal and transverse sections, presented a very cellular appearance, owing to the presence of many endothelial cells among the fibres and to a possible increase in connective tissue nuclei. The appearance suggested an actual proliferation probably originating in the cells lining the perineural lymphatics. The fibres in the smaller nerves seen in longitudinal section were frequently widely separated, suggesting the presence of œdema inside the bundles. It is notable that the larger intramuscular nerves showed no infiltrative or proliferative change whatever.

The intramuscular nerves of the diaphragm did not possess the dilated perineural lymph spaces, nor was there any proliferative change in the nerves of this muscle.

Transverse sections of the muscles stained by the Weigert-Pal method showed the intramuscular nerves to be deprived of their myelin in varying degree. Many of the nerves in all the muscles except the diaphragm contained a large number of the fibres entirely without myelin. However, considerable variation existed in the individual muscles, some of the nerves having little less than the normal amount, whereas certain bundles were almost entirely demyelinated. In longitudinal sections beading and irregularity of the myelin were very pronounced in most of the nerves.

The most severe degeneration was seen in the nerves of the biceps brachialis. Those in the biceps femoris were a little less affected and the nerves in the erector spinæ had less myelin loss than the two former muscles, although in many of the nerves it was quite severe. The nerves of the diaphragm were well myelinated, although here also some beading and irregularity were observed.

The sensory nerves in the muscle spindles were, for the most part, well myelinated. In a few instances the myelin was absent, but in general it was far better preserved in these fibres than in the motor nerves.

Around some of the muscle spindles dilated spaces were seen similar to those surrounding the motor intramuscular nerves.

SPINAL CORD.—Technique: After ten days' fixation in 10 per cent. formol saline, sections were cut at various levels on the freezing microtome and stained by the Marchi method and Scharlach R.

Pieces from every segment of the cord were embedded in celloidin and sections cut from each segment were stained by the following methods: Loyez's stain for myelin, hæmatoxylin and van Gieson, toluidin blue. Sections from every alternate segment were stained by the Weigert-Pal method.

Microscopic examination.—Despite careful examination, no degeneration of the white matter was observed in the cord. The cells of the anterior horns, however, varied definitely from the normal shape and presented a rounded appearance throughout the cervical, thoracic and lumbar segments. Many cells in the cervical and thoracic regions were so shrunken in size that at first glance the cells were thought to be diminished in number in all the cell groups. A count of the cells showed that the actual diminution in number was slight, though in places many of the cells were so small as to be only just recognizable as such. The segments possessing the largest numbers of shrunken cells were C. 7, Th. 3, 6, 7, 8 and 9. In the remaining cervical and thoracic segments the cells were considerably nearer to the normal in size, and in the lumbar and sacral regions there was practically no evidence of shrinkage.

The nuclei of the cells were normally situated and no true chromatolysis was present. The Nissl granules, however, were large and irregular in size in the rounded cells and in many instances tended to clump in the centres of the cells, leaving a narrow clear area of cytoplasm at the periphery (fig. 8). These changes in the Nissl granules were most obvious in the thoracic segments, but they were also present in varying degree in segments C. 3, 6, 7 and 8 and L. 1 and 2. No abnormality of the Nissl granules was seen in the remainder of the cord. No excess of normal yellow pigment was present in the cells. The cells of Clarke's column were normal.

A great increase in vascularity was present throughout the grey matter. The vessels were much more numerous than is normally the case and were dilated and engorged with blood corpuscles. The walls of many of the vessels were thickened by an increase of connective tissue, but no proliferation of the intimal lining was present.

DORSAL ROOT GANGLIA.—Technique: After fixation with the cord, ganglia from the cervical, thoracic and lumbar regions were imbedded in paraffin and sections were stained with hæmatoxylin and van Gieson, toluidin blue and Mallory's anilin blue-Orange G. stain.

Microscopic findings.—No abnormality was observed in the size or shape of the cells. The nuclei were centrally situated and no chromatolysis was present. There was a definite thickening of the capsules surrounding many of the cells due to a proliferation of capsule cells. This change was most apparent in the ganglia from the thoracic region.

ANTERIOR AND POSTERIOR NERVE ROOTS.—Technique: The same technique was employed as for the spinal cord.

Microscopic findings.—Hæmatoxylin and van Gieson-stained sections revealed little, if anything, abnormal in the posterior roots except an increase in vascularity. In the anterior roots the increase in vascularity was greater and a few mononuclear cells were seen amongst the nerve fibres. No advanced proliferative or infiltrative changes were present in the nerve roots such as were seen in the peripheral nerves.

Weigert-Pal sections presented a striking picture. The posterior roots were all normally myelinated except in one or two of the thoracic segments where slight loss was evident in portions of the roots at some distance from the cord. The anterior roots, however, had extensive myelin loss throughout the lower cervical, thoracic and upper lumbar regions of the cord. This varied in degree in different segments but it was well marked in all, and in a number of the lower cervical and thoracic segments the proportion of demyelinated fibres equalled that found in the peripheral nerves (fig. 9).

In the roots of the cauda equina no infiltrative or proliferative changes were present. No myelin degeneration was seen in these roots stained by the Marchi method.

BRAIN.—Technique: After ten days' fixation in 10 per cent. formalin saline frozen sections were cut from the prefrontal lobe and the precentral and post-central convolutions. The sections were stained with Scharlach R., toluidin blue and Bielschowsky's stain for neurofibrils.

Microscopic findings.—The sections revealed no abnormality in the cells or neurofibrils and no increase in the deposition of fat.

MEDULLA.—Technique: After fixation with the brain the medulla was imbedded in celloidin and serial sections were cut through its entire length. Every tenth section was stained with hæmatoxylin and van Gieson and toluidin blue.

Microscopic findings.—No abnormality was present in any of the cell groups. The cells of the dorsal nucleus of the vagus and the nucleus ambiguus were normal in size and appearance. Great increase in vascularity was evident throughout the medulla; the vessels were extremely numerous and engorged with blood.

The greatest increase in vascularity existed in the region occupied by the dorsal nucleus of the vagus, and in two places, at considerable distance apart, moderately large, fresh hæmorrhages were seen amongst the cells of this nucleus.

A slight perivascular infiltration of mononuclear cells existed throughout the medulla.

MUSCLES.—*Technique*: The methods used for the muscles was described when the intramuscular nerves were considered.

Microscopic findings.—Measurement of the fibres and comparison with normal muscles revealed that the fibres of the biceps brachialis, biceps femoris and erector spinæ were very much reduced in size. The great majority of the fibres in the biceps brachialis were between 15 and 30 μ in diameter; in the other two muscles they averaged a little larger. All three muscles contained many very small fibres however, and fibres 5 to 10 μ in diameter were frequently seen. Occasionally amongst the atrophied fibres were little groups of large fibres varying in size from 60 to 110 μ in their smallest diameter, but these were not common in the muscles. The fibres of the diaphragm averaged little if at all less than the normal size; no gross irregularity in size or shape was evident.

The fibres in all the muscles were well striated, and apart from atrophy no other abnormality was observed. A moderate increase of connective tissue was seen in all the muscles except the diaphragm. There was no increase in the sarcolemma nuclei.

PLATE XV.

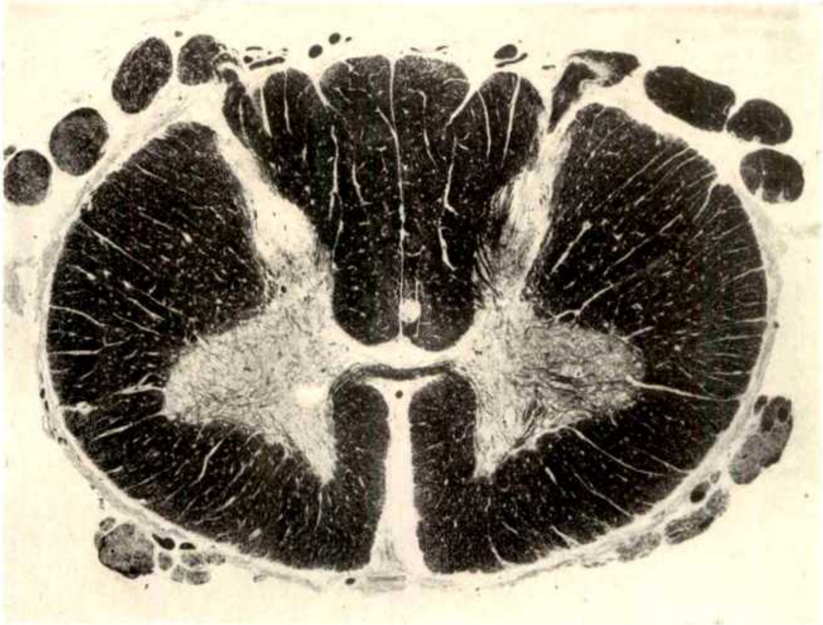

FIG. 9.—Ninth thoracic segment—low power. The posterior roots are well myelinated, whereas advanced degeneration is present in both anterior roots. Weigert-Pal (celloidin section).

To illustrate paper by Herbert H. Hyland and W. Ritchie Russell

The diaphragm was extensively infiltrated with little groups of small round cells. These usually surrounded small blood-vessels lying between the muscle fibres. A very much less extensive infiltration was present in the other three muscles. Small groups of mononuclear cells were seen in the connective tissue spaces or between the muscle fibres, having no relation to blood-vessels. Occasionally a group of these cells was adjacent to one of the small nerves in which endothelial proliferation was occurring.

SUMMARY OF PATHOLOGICAL FINDINGS.

The body of a well-nourished woman with no gross atrophy except moderate wasting of the fore-arms. The nerves in the upper limbs were definitely larger than normal and the cord in the thoracic region appeared rather softened. Apart from broncho-pneumonia and partial collapse of the right lung no other changes of importance were noted outside the nervous system.

Microscopic examination of the nervous system revealed that the anterior horn cells in the spinal cord were rounded and shrunken. The Nissl granules were pyknomorphic and had a tendency to clump in the centres of the cells. No actual chromatolysis was present and there was no degeneration of the white matter in the cord.

The anterior nerve roots, the peripheral nerves and the intramuscular nerves were severely demyelinated. The posterior nerve roots were very slightly affected in this respect and the sensory nerves in the muscle spindles had relatively less myelin loss than the motor intramuscular nerves. The only purely sensory nerve examined, the internal cutaneous, had less myelin degeneration present than the other peripheral nerves.

All the peripheral nerves showed proliferation of the interstitial tissue and were infiltrated by mononuclear cells.

Two interesting findings in the intramuscular nerves of the muscles of the back and limbs were a dilatation of the perineural lymph spaces and a proliferation of endothelial cells inside the small nerve bundles where the latter lay in groups between the muscle fibres.

Many of the cell capsules of the dorsal root ganglia were definitely thickened by proliferation of the capsule cells.

Nothing abnormal was found in the brain and the medulla was normal apart from great increase of vascularity and two recent hæmorrhages amongst the cells of the dorsal nucleus of the vagus.

In the muscles of the limbs and back there was severe generalized atrophy of the fibres. The diaphragm was not atrophied but extensive perivascular infiltration by mononuclear cells was present.

Commentary.—Polyneuritis arising from various causes may progress slowly, but the great majority of cases show remissions or become arrested before paralysis is extreme. A clinical course similar to that in the case described is particularly unusual. The type is, however, probably identical with that described by Harris [4], although his cases recovered from the extreme paralysis which occurred. The fatal termination in this case provided a valued opportunity for one of us (H.H.H.) to investigate its pathology.

Various changes have been described in the spinal cords of cases of peripheral neuritis. In the white matter the posterior columns are most frequently affected, as has been emphasized by Herzog [5] and Cole [2]. The latter, indeed, after an extensive search of the literature up to 1902, found no record of a case in which the cord failed to show degeneration of these columns if the Marchi method had been employed.

Where changes have been found in the anterior horn cells, they have usually consisted of a varying degree of central chromatolysis with displacement of the nuclei to the periphery of the cell.

Grinker, in 1907 [3], expressed the view that cases of polyneuritis usually showed no changes either in the cord or anterior roots. Pfeifer [7], however, more recently re-emphasizes the frequency with which changes are found in both white and grey columns of the cord and also in the brain.

It should be noted that very different types of polyneuritis have been included in these observations. Grinker's case resembled in many ways the case here described, especially in its clinical course, but the pathological examination (which was incomplete) showed no cord changes.

In the present case an exhaustive search revealed no trace of degeneration in the white matter of the cord, nor were there any changes detected in the brain. In the grey matter the changes found in the anterior horn cells resembled in many respects those found in progressive muscular atrophy. The changes in the Nissl granules presented a somewhat similar picture to those described by Martin [6] in cases of syphilitic progressive muscular atrophy.

The changes in the peripheral nerves were similar to those found in other types of severe polyneuritis. The predominance of motor as compared to sensory nerve involvement was prominent both clinically and pathologically and corresponded to the clinical findings in Harris's cases.

As regards the ætiology of this type of neuritis, Harris suggests that the slow development in such cases indicates a continuously acting toxin rather than an acute poisoning, and that one is driven to the supposition that an auto-toxæmia is at work. In his second case the absorption of external toxins could probably be excluded, as the patient continued to get weaker for nine months after returning from South Africa to England. In the case here considered, this factor could probably also be excluded as her downward progress was uninterrupted during a stay of seven weeks in hospital.

Cases have occurred following acute illnesses, such as that described by Barnes (*vide supra*) which followed rheumatic fever. It is noteworthy that both one of Harris's cases and the present case developed after a dermatitis of doubtful nature.

The dilatation of perineural lymphatic spaces which was an interesting factor in this case was also noted by Stewart [9] in a case of fatal puerperal polyneuritis and poliomyelitis. In his case the changes were found in the large nerve trunks, whereas in this case they were most marked in the intramuscular branches.

We wish to express our thanks to Dr. James Collier and to Dr. Russell Brain for permission to publish the case; and to acknowledge our indebtedness to Dr. J. Godwin Greenfield for his assistance with the pathological investigation and for taking the photomicrographs.

SUMMARY.

(1) A case of polyneuritis which ran a progressive course and terminated fatally in twelve months is reported.

(2) Somewhat similar cases are referred to.

(3) A pathological study of the case is described (see Summary of Pathological Findings).

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VASCULAR LESIONS OF THE HIND-BRAIN. (LATERAL MEDULLARY SYNDROME.)[1]

BY HOUSTON MERRITT, M.D.
AND
MAXWELL FINLAND, M.D.

VASCULAR lesions of the lateral portion of the medulla are generally known as the syndrome of the occlusion of the posterior inferior cerebellar artery. This syndrome was first described by Wallenberg [1] in 1895, although very similar cases were reported by Senator [2] eleven years previously. Since the first description there have been a limited number of cases reported, chiefly in the French literature. Xavier Combes [3] in 1902 reviewed eight cases of the syndrome, including the cases reported by Babinski and Nageotte, Cestan and Hoffman, Foix, Hillemand and Schalit [4] in 1925 reported a case and analysed sixteen previously reported cases from the standpoint of the blood-vessel involved. Their conclusions will be mentioned later. In the American literature the subject has received attention from H. M. Thomas [5] in 1907, W. G. Spiller [6] in 1908, G. W. Robinson [7] in 1913, R. H. Thompson [8] in 1929, and W. H. Riley [9], in 1930. In the English literature cases have been reported by Menzies [10] in 1893, S. A. K. Wilson [11] in 1909, Wilfred Harris [12] in 1910, and Ramsbottom and Stopford [13] in 1924.

The syndrome is supposed to be comparatively rare, but at the Boston City Hospital we have met six cases in the past two years, and Riley [9] of Battle Creek, Michigan, encountered eight cases in a similar period. It is probable, therefore, that the syndrome is fairly common.

The following six cases were observed at the Boston City Hospital during the years 1928 and 1930. As far as we are able to determine four of these patients are still living. Two of the patients died while in the hospital, and post-mortem examination was made on one of these.

---

[1] Read before the Boston Society of Psychiatry and Neurology, February 20, 1930. From the Second Medical and Neurological Services of the Boston City Hospital, and the Department of Neuropathology, Harvard Medical School, Boston, Mass.

A summary of the history and abnormal findings in these cases is as follows :—

Case 1.—James L., aged 69, retired salesman, admitted December 15, 1927, to the Second Medical Service of the Boston City Hospital. He died March 15, 1928. His chief complaints were vertigo and dysphagia.

Family history and past history were not important except that he had a "stroke" in 1913, resulting in a paralysis of the left arm and leg. He recovered rapidly without any residual paralysis.

Present illness.—On the morning of December 14, the patient became nauseated and vomited, and felt very dizzy. He did not lose consciousness, however, and was helped into a taxi-cab. He went home and went to bed. He then began to notice a sharp pain in the central portion of the right half of the face. The dizziness persisted and he vomited several times more. In the afternoon he found that he could not swallow, and that foods and liquids regurgitated through his nose. He also noticed diplopia. On the advice of his physician he presented himself at the hospital the following day and was admitted.

Physical examination.—The peripheral vessels were moderately sclerosed and his blood-pressure was 164/100.

Neurological examination on admission showed the following abnormalities (see fig. 1) :—

Cranial nerves :—

(1) There was a mild Horner's syndrome on the right (i.e., enophthalmos, myosis, and drooping of the lid with narrowing of the palpebral fissure).

(2) The eye movements were normal, but there was a well-sustained horizontal nystagmus, more marked on right lateral deviation.

(3) There was impairment of light touch and pain sensation in the distribution of the right trigeminal nerve.

(4) There was definite, although slight, weakness of the right half of the face.

(5) His voice was hoarse, and swallowing was very difficult. The palate deviated to the left on phonation.

Motor system.—No disturbance of the motor system could be detected.

Sensory system.—There was impairment of sensation to light touch and pain in the left arm and leg. Other forms of sensation were not tested.

Reflexes.—The deep reflexes were more active on the left side. The plantar responses were normal. The abdominal reflexes were absent.

Laboratory data.—The urine and blood were normal. The blood Wassermann test was negative.

Course in the hospital.—The sensation of dizziness cleared rapidly and the dysphagia disappeared in the course of a month. The hoarseness persisted for about ten weeks. The Horner's syndrome was much less noticeable after a few weeks but persisted until death. During the first few days after admisssion the patient was troubled with intractable hiccoughing. Eleven weeks after admission the patient developed erysipelas on the right side of the face, and died eight days later.

The *pathological findings* at necropsy were broncho-pneumonia, erysipelas, marked arterio-sclerosis, and chronic vascular nephritis. The brain (N-28-9) showed marked sclerosis of the basilar vessels, but no detailed study of them was made. The cerebrum appeared normal on gross examination. The medulla was sectioned serially.

The sections of the medulla showed a mild degeneration of the pyramidal tract on the right side. This extended through all the sections, and was separated from the lesion in the lateral portion of the medulla; it was considered to be the result of the "stroke" in 1913. The interesting lesion, however, was a triangular area of degeneration in the lateral portion of the medulla extending from just above the cuneate and gracile nuclei to the level of the entrance of the restiform body into the cerebellum. It involved the lateral reticular substance and destroyed the nucleus ambiguus, the oculo-pupillary nucleus, the spinal lemniscus, the descending nucleus and tract of the trigeminal nerve, and the lateral reticular nucleus. In the lower sections there was a slight involvement of the extreme lateral portion of the restiform body. A small portion of the dorso-lateral edge of the olivary nucleus was also destroyed. The hypoglossal nerve nucleus and the medial lemniscus were not involved. The lower end of the tractus solitarius was destroyed.

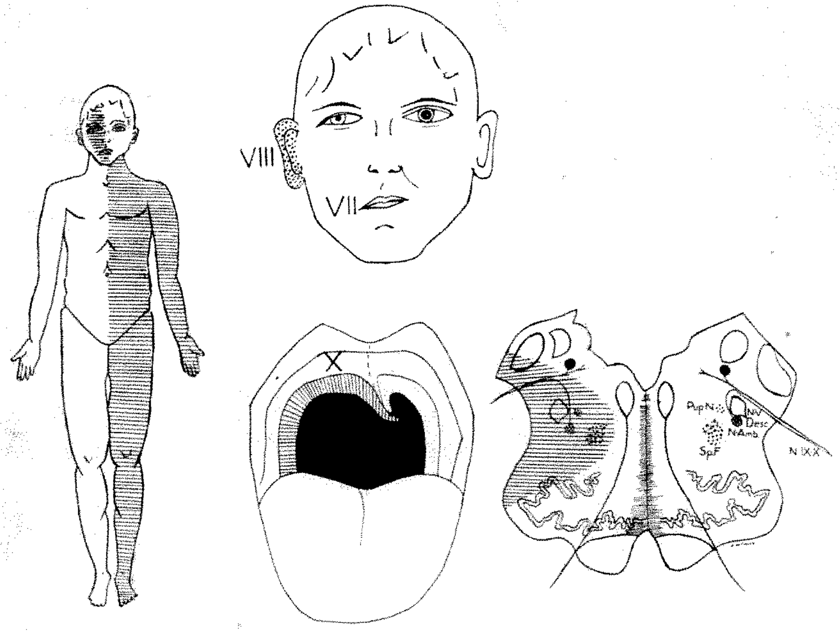

FIG. 1 (*Case* 1).—Sketch showing cranial nerves injured, the distribution of the sensory changes and the approximate location of the lesion in the medulla.

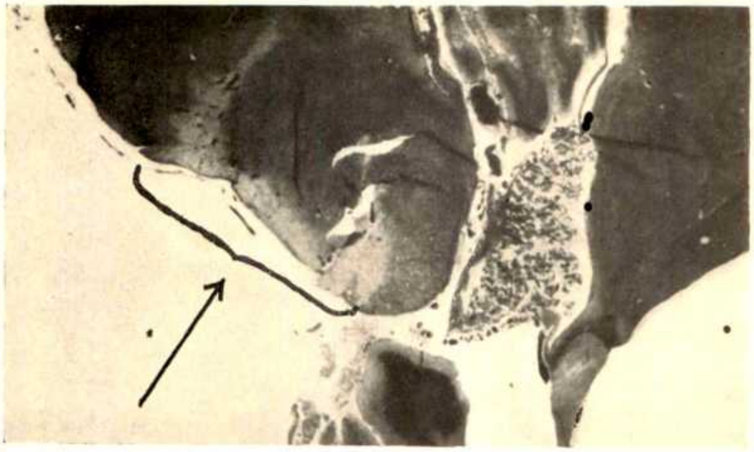

FIG. 2 (*Case* 1).—Photograph of section of the right side of the medulla showing the lower level of the lesion. The degenerated area lies chiefly in the restiform body and in the lateral reticular substance. Weigert's stain.

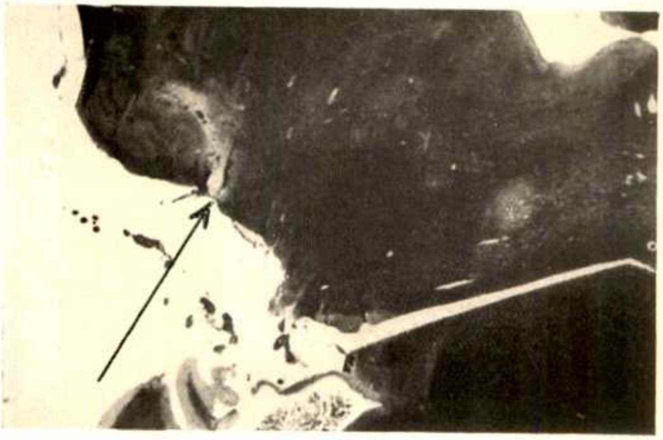

FIG. 3 (*Case* 1).—Photograph of section of the right side of the medulla showing the central portion of the lesion. The area of degeneration is confined to the lateral reticular substance. Weigert's stain.

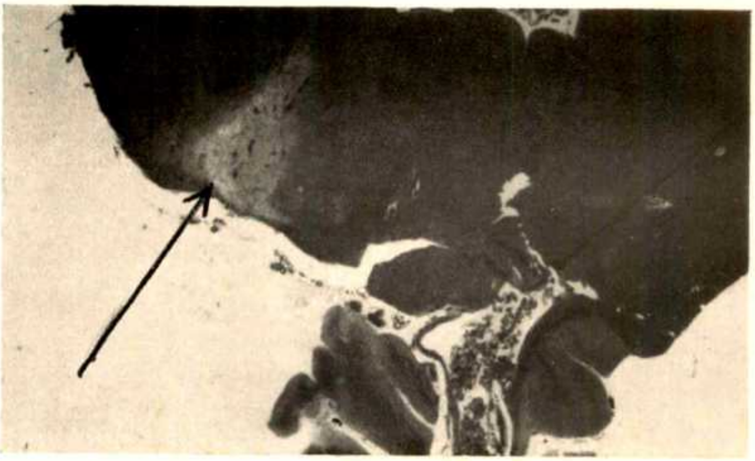

FIG. 4 (*Case* 1).—Photograph of section of the right side of the medulla showing the upper level of the lesion. The area of degeneration lies in the lateral reticular substance and involves the dorsal portion of the olivary nucleus. Weigert's stain.

To illustrate paper by Houston Merritt and Maxwell Finland.

Figs. 2, 3 and 4 show photographs of sections taken from the lower, central and upper levels of the lesions, respectively.

Case 2.—Estelle W., aged 69, widow, unemployed, admitted to the Second Medical Service of the Boston City Hospital October 10, 1927, and discharged April 29, 1928, as improved.

The patient had been receiving treatment in the out-patient department of the hospital for a period of about seven years on account of chronic nephritis and hypertension. On October 10, 1927, she was accidentally overcome by coal gas, and was brought to the hospital. She recovered rapidly from the gas poisoning, but remained in the hospital for treatment of her nephritis.

On January 14, 1928, while still in the hospital, she complained of a severe pain over left side of her face, and also of marked dizziness, and diplopia. These symptoms persisted, and the following day herpetic lesions appeared on the lips, and she became unable to swallow, food regurgitating through her nose. Her voice became husky and she had intractable hiccoughing. She complained of pain in the left side of her throat, and a cold sensation with numbness on the left side of face and right side of the body.

Physical examination.—The heart was moderately enlarged, the peripheral vessels were sclerotic and the blood-pressure was 260/100.

Neurological examination on January 16, 1928, showed the following abnormalities (see fig. 5):—

Cranial nerves :—

(1) There was a left-sided Horner's syndrome.

(2) The eye movements were of normal range, but the patient complained of diplopia on looking to the left.

(3) There was an impairment of the light touch and pain sensibility on the left side of the face.

(4) The voice was husky and there was marked dysphagia. The palate deviated to the right on phonation.

There was marked dizziness, but no nystagmus or impairment of hearing was noted.

Motor system.—There was a very slight weakness of the right arm and leg.

Sensory system.—There was hypæsthesia (modalities not noted) of the skin of the right arm and leg with a subjective sensation of numbness and tingling.

Reflexes.—The deep reflexes were more active on the right side than on the left. The abdominal and plantar reflexes were normal.

Laboratory data.—The urine showed the changes found in chronic nephritis. The blood-count was normal, and the blood Wassermann was negative.

Course in the hospital.—Patient was discharged from the hospital about three and a half months after the vascular accident. The hoarseness had disappeared, and there was only slight dysphagia. There was still slight weakness of the left half of the face and of the right arm and leg. The subjective numbness and objective sensory changes persisted. Horner's syndrome had disappeared.

Case 3.—Mary J., aged 61, housewife, admitted to the First Medical Service of the Boston City Hospital, November 18, 1928. She was discharged December 23, 1928, as improved. Her chief complaints were dizziness, dysphagia and hoarseness.

Family history and past history were irrelevant.

Present illness.—The patient had been under treatment for hypertension, and on November 17 she went to her physician to consult him about constipation. While there she suddenly became unconscious and fell to the floor. She regained consciousness in about twenty minutes and noted a pain in the left side of her head and a sensation of coldness and numbness in the right arm and leg. Her voice was husky and she had great difficulty in swallowing, liquids and solids regurgitating through her nose. These symptoms persisted and she was permitted to the hospital on the following day.

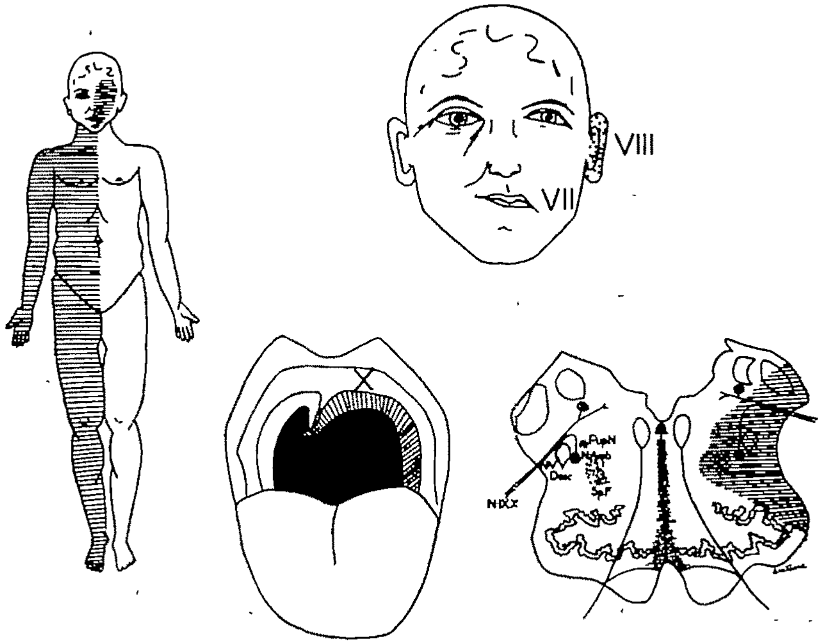

FIG. 5 (*Cases* 2 and 3).—Sketch showing the cranial nerves injured, the distribution of the sensory changes, and the approximate location of the lesion in the medulla.

Physical examination.—The heart was enlarged and was irregular in rhythm owing to premature systoles. The peripheral vessels were sclerosed and the blood-pressure was 180/100. The blood and urine were normal and the blood Wassermann reaction was negative.

Neurological examination on admission showed the following abnormalities (see fig. 5):—

Cranial nerves :—

(1) Horner's syndrome on the left side.

(2) There was limitation of movement of the eyes to the extreme left and patient complained of diplopia on looking to the left.

(3) There was impairment of sensation to pain and temperature in the distribution of the left trigeminal nerve. The left corneal reflex was absent and there was a very slight weakness of the masticatory muscles on the left side.

(4) There was a slight weakness of the left half of the face involving both upper and lower portions.

(5) There was horizontal nystagmus, subjective vertigo and lateropulsion to the left.

(6) The voice was husky. There was marked dysphagia and the palate deviated to the right on phonation.

The motor system was normal.

Sensory system.—There was impairment of sensation to pain and temperature in the skin of the right arm, trunk and leg. Light touch, vibratory and position sense were normal. There was a subjective sensation of numbness of the right arm, trunk and leg.

Reflexes.—The deep reflexes and the plantar responses were normal. The abdominal reflexes were absent on the left side.

Course in the hospital.—The patient remained in the hospital for five weeks. At the end of this time she was able to swallow without difficulty and her voice was much less husky. The subjective vertigo and the lateropulsion had disappeared. The Horner's syndrome and the sensory changes were still present, however.

Case 4.—Catherine S., aged 75, unmarried and unemployed, admitted November 3, 1929, to the First Medical Service of the Boston City Hospital. She died November 13, 1929.

Her chief complaints were difficulty in swallowing, dizziness and sudden weakness.

Family history and past history were not important. The patient had ceased work nine years previously, and since that time had remained at home. For the past year or more she had complained of increasing weakness and fatigability.

Present illness.—The patient awoke October 30, 1929, and attempted to get out of bed. She fell back unconscious and remained so about half an hour. On gaining consciousness she was very dizzy and she had great difficulty in swallowing. Her voice was husky. She was brought to the hospital four days later and a connected story of her illness was difficult to obtain as there was a definite impairment of her memory.

Physical examination.—Patient was an obese white woman. The heart was enlarged and the rate was rapid and irregular. The peripheral vessels were sclerotic and the blood-pressure was 150/100.

Neurological examination on admission showed the following abnormalities (see fig. 6):—

Cranial nerves :—

(1) There was a Horner's syndrome on the right side.

(2) There was a weakness of the right half of the face involving both the upper and lower portions.

(3) There was slight horizontal nystagmus.

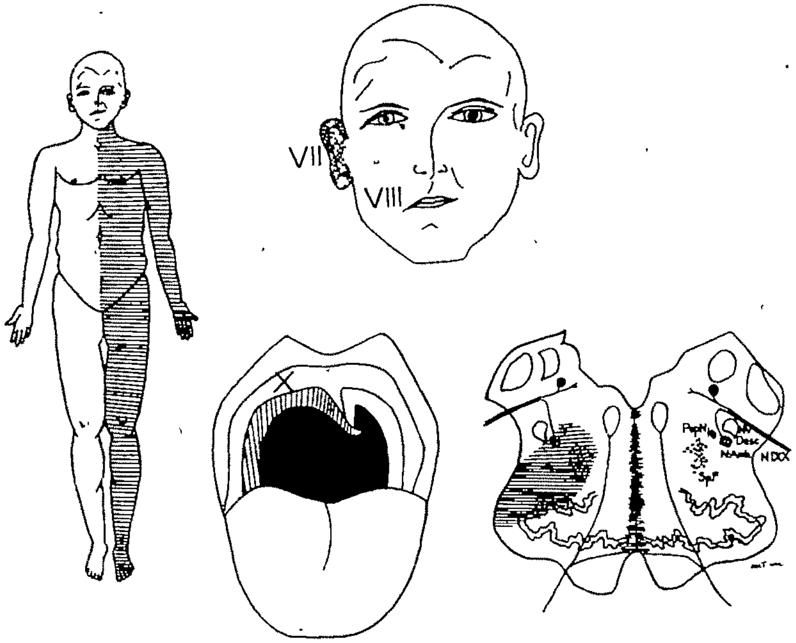

FIG. 6 (*Case* 4).—Sketch showing the cranial nerves injured, the distribution of the sensory changes, and the approximate location of the lesion in the medulla. (In the full face diagram the Roman figures VII and VIII should be transposed.)

(4) The voice was hoarse, and there was marked dysphagia. The palate deviated to the left on phonation.

(5) The right corneal reflex was absent. There was no loss of any of the forms of cutaneous sensation in the face.

Motor system.—There was a marked generalized weakness, equal on the two sides.

Sensory system.—Sensation to pain and temperature was impaired in the left arm, trunk and leg. There was no impairment of the light touch, vibratory or position sense. The patient complained of a sensation of numbness in the left arm and leg.

Reflexes.—All of the deep reflexes were markedly diminished. The abdominal reflexes were absent. The plantar responses were normal.

Laboratory data.—The blood and urine were normal. The blood Wassermann test was negative. The cerebrospinal fluid was under a pressure of 240 mm. of water. It was clear and colourless and contained 5 lymphocytes per cubic mm. The total protein content was 50 mgm. per 100 c.c. The colloidal gold and Wassermann tests of the fluid were negative.

Course in the hospital.—The patient gradually became more feeble, the heart's action weakened and she died on November 13, 1929, ten days after admission.

Case 5.—Annie D., aged 43, housewife, admitted February 1, 1930, to the Third Medical Service of the Boston City Hospital and transferred to the Neurological Service. She was discharged April 13, 1930, as improved.

Her chief complaints were inability to swallow and numbness of the left half of face and body.

Past history and family history were irrelevant.

Present illness.—On January 26, 1930, the patient was confined to bed with a cold. Four days later, she attempted to get out of bed and suddenly became dizzy. The room seemed to be "spinning around," and it was necessary for her to hold on to a table to avoid falling. Her head began to ache and she noticed a ringing in her right ear. On looking to the right objects appeared double. All these symptoms persisted, and about two days later she noticed a numbness and tingling of the left side of her body, beginning in the arm, spreading downward to the leg and foot, and finally involving the left half of the face. Later in the day she became unable to swallow her own saliva and she was sent to the hospital by her physician.

Physical examination.—The heart was enlarged especially to the left, and the typical murmurs of mitral and aortic valve lesions were heard. The rate and rhythm were normal. The blood-pressure was 135/85. The abnormality of the heart was considered as being rheumatic in origin.

Neurological examination on admission showed the following abnormalities (see fig. 7):—

Cranial nerves:—

(1) Horner's syndrome was present on the right side.

(2) The ocular movements were of normal range but the patient complained of diplopia on right lateral deviation.

(3) There was a loss of pain and temperature sensation in the distribution of the right trigeminal nerve. The right corneal reflex was absent.

(4) The right face was slightly weak in both the upper and lower portions

(5) There was slight impairment of hearing of the nerve deafness type in the right ear. There was lateral and vertical nystagmus. Patient complained of a ringing in the right ear, and a dizziness when looking to the right. There was slight lateropulsion to the right.

(6) There was extreme difficulty in swallowing. The palate deviated to the left on phonation.

Motor system.—The right arm and leg were slightly weak and hypotonic. There was intention tremor, inco-ordination, cerebellar rebound and past pointing on the right side.

Sensory system:—

(1) There was a subjective sensation of numbness of the entire left half of body, including face, arm, trunk and leg.

(2) Sensation to pain and temperature was lost in the skin of the left half of the body, including the face. There was loss of the pain and temperature sensibility in the right trigeminal nerve distribution, as noted above. When the left side of the body was touched with a hot or cold object or with a pin the patient complained of a "peculiar sensation," which was disagreeable and uncomfortable, but she was unable to describe it further.

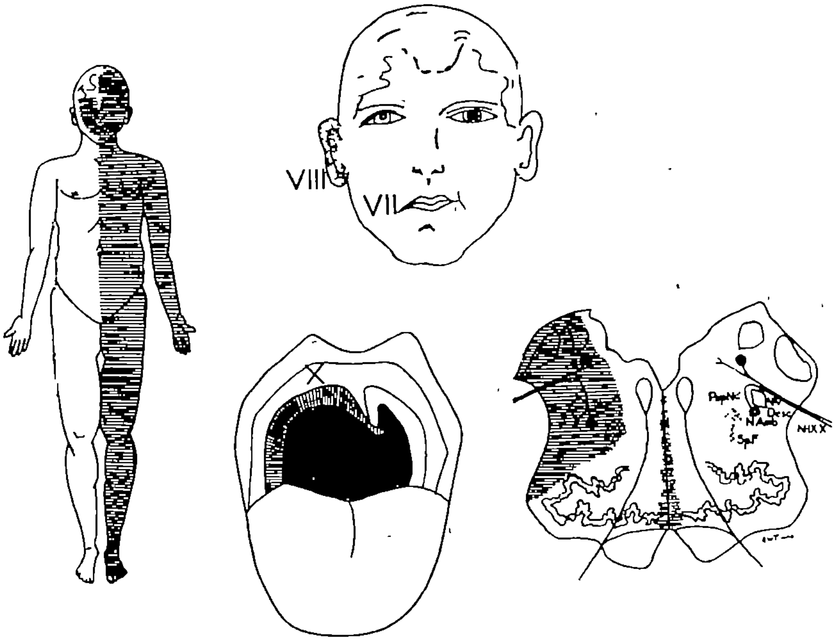

FIG. 7 (*Case 5*).—Sketch showing the cranial nerves injured, the distribution of the sensory changes, and the approximate location of the lesion in the medulla.

(3) Sensation to light touch (cotton) was present everywhere, but patient stated that she felt it better on the right half of the body.

(4) There was loss of the sense of taste on the right half of the tongue.

(5) Vibration and position sense were normal.

Reflexes.—The left knee-jerk was slightly hyperactive, and the plantar response was absent on the left side. The abdominal reflexes were normal.

Laboratory data.—The blood and urine were normal. The blood Wassermann test was negative. The spinal fluid was under pressure of 150 mm. of water. It was clear and colourless, with no cells. The total protein content was 10 mg. per 100 c.c. The colloidal gold was 1112110000, and the Wassermann test was negative.

Course in the hospital.—The patient improved gradually and when discharged on April 13, 1930, she could swallow liquids and solids without difficulty. The dizziness and cerebellar ataxia had disappeared and she was able to walk well. There was only slight nystagmus on discharge and no weakness of the facial muscles could be detected.

Horner's syndrome was still present and the sensory findings were the same as on admission.

Case 6.—Oscar C., aged 56, negro, engineer, admitted November 18, 1929, to the Neurological Service of the Boston City Hospital, and discharged February 16, 1930, as improved.

His *chief complaint* was inability to talk or swallow.

Family history and past history were irrelevant.

Present illness.—The patient went to work on November 18, 1929, as usual. His helper stated that he seemed quieter than usual and that he was perspiring profusely. He was working with an electric drill and suddenly, without turning it off, he handed it to his helper. He began rubbing the left side of his face and walked outside into the rain. His helper followed and asked what was the difficulty. The patient continued to rub the left side of his face and did not answer. When the question was repeated the patient finally managed to say "I think I have had a stroke." He was brought to the hospital immediately,

Physical examination—The patient was obese and plethoric. The heart was enlarged to the left and the blood-pressure was 170/100.

Neurological examination.—The following abnormalities were present at time of admission (see fig. 8):—

Cranial nerves:—

(1) There was a Horner's syndrome on the left side.

(2) There was loss of all forms of sensation in the distribution of the left trigeminal nerve. The left corneal reflex was absent, and there was a paralysis of the muscles of mastication on the left.

(3) The left abducens nucleus was paralysed. The patient was unable to look to the left.

(4) There was complete paralysis of the facial muscles on the left side.

(5) There was slight impairment of hearing of the nerve type in the left ear, and there was marked horizontal and vertical nystagmus.

(6) There was moderate dysphagia and extreme dysarthria, his speech being barely intelligible. The palate deviated to the right on phonation.

Motor system.—There was weakness, inco-ordination, ataxia, and intention tremor of the left arm and leg.

Sensory system :—

(1) Patient complained of numbness of the entire right side of his body (face, arm and leg).

(2) There was loss of pain and temperature sensation in right leg, trunk, arm and face.

(3) Light tactile stimuli were readily recognized, but the patient stated they were felt better on the left side than on the right.

(4) Vibration and position sense were normal.

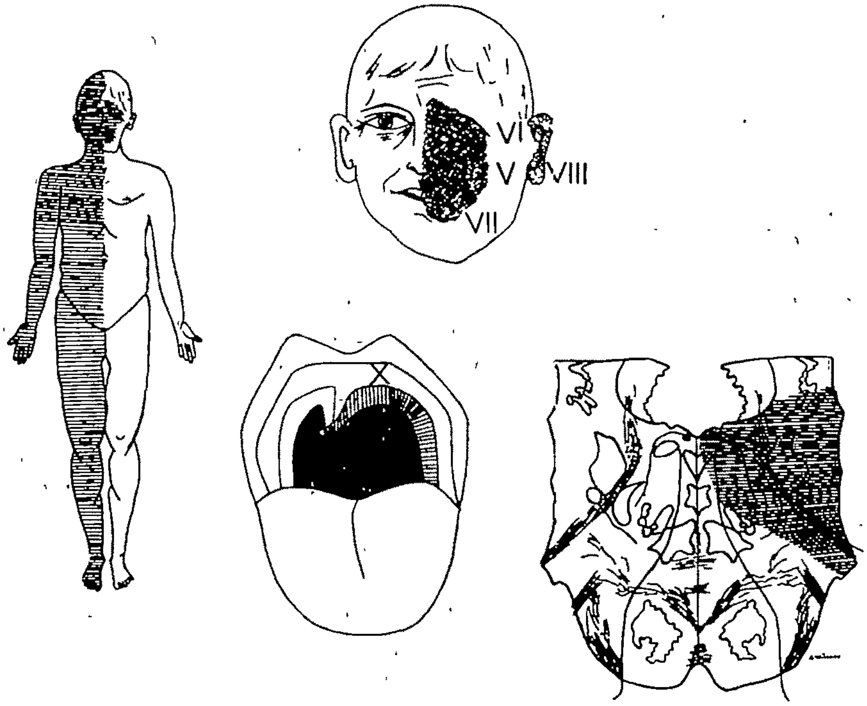

FIG. 8 (*Case* 6).—Sketch showing the cranial nerves involved, the distribution of the sensory changes, and the approximate location of the lesion in the medulla.

Reflexes.—All the deep reflexes were markedly diminished. The right plantar response was equivocal. The abdominal reflexes were normal.

Laboratory data.—The urine and blood were normal. The blood Wasserman test was negative.

The cerebrospinal fluid on the day of admission was under a pressure of 240 mm. of water. The fluid was blood-stained and contained 200,000 red blood-corpuscles and 400 white blood-corpuscles per cubic mm., 80 per cent. of the latter being polymorphonuclear leucocytes, and 20 per cent lymphocytes. The total protein content was 800 mg. per 100 c.c. The colloidal gold test was 0011112233, and the Wassermann test was negative. One week later the pressure was 200 mm. of water. The fluid was xanthochromic and contained 4,500 red blood-corpuscles, and 555 white blood-corpuscles. The total protein content was 148 mg. per 100 c.c., and the colloidal gold and Wassermann tests were negative.

Course in the hospital—The patient developed a keratitis and pan-ophthalmitis in the left eye which was enucleated on December 16. He was discharged on February 16, 1930, at which time there was obvious atrophy of the masticatory muscles on the left side. The paralysis of the left facial muscles was still complete. The dysarthria had improved markedly, the function of the right internal rectus muscle had returned, and the patient was able to look to the left with the right eye. The patient could walk, but there was still considerable ataxia of the left arm and leg. The sensory changes persisted.

DISCUSSION.

The cases here presented are very similar to those previously reported. The lesion occurs generally in arterio-sclerotic individuals and the age of onset in our cases, as shown in Table I, was in the sixth or later decades, except in Case 5, where the lesion could be explained on basis of an embolus from a rheumatic heart. A few cases have been reported in young individuals, but usually in syphilitics.

The onset is generally fairly sudden without loss of consciousness, and is often followed by a period during which there is an increase in the symptoms.

TABLE I.—SYMPTOMS.

Case	Age and Sex	Time of progress *	Pain in face	Diplopia	Vertigo	Nausea	Dysphagia	Dysarthria	Subjective numbness
1	69 M.	12 hours	+	+	+	+	+	+	0
2	69 F.	24 hours	+	+	+	0	+	+	+
3	61 F.	Sudden	+	?	+	0	+	+	+
4	75 F.	Sudden	0	?	+	0	+	+	+
5	43 F.	48 hours	+	+	+	+	+	0	+
6	56 M.	Sudden	+	+	+	+	+	+	+

* Time from onset to full development of symptoms.

The symptoms, as shown in Table I, can readily be explained by the neurological lesion, and are accompanied by objective evidence of this involvement as illustrated by Table II. Of the symptoms only vertigo and dysphagia were present in all cases. Pain in the homolateral side of the face, subjective numbness on the contralateral side and dysarthria were present in five of the cases. Diplopia was complained of by four, and cerebellar symptoms were present in three cases. Intractable hiccoughing was present in only two cases.

The neurological signs accompanying these symptoms (see Table II) were as follows: All of the cases showed objective signs of involvement of the spinal fillet, nucleus ambiguus, facial nerve nucleus and the pupillary centre in the medulla. The eighth-nerve nuclei were involved in five of the cases and the cerebellar pathways in three. The descending nucleus and tract of the trigeminal nerve were involved in five of the cases while the main sensory nucleus and motor nucleus of the trigeminal nerve were involved in only one case (Case 6). The abducens nucleus was involved in this case also, and considering the extent of the damage and the finding of blood in the cerebrospinal fluid, it is probable that the lesion was a hæmorrhage rather than a thrombosis.

TABLE II.—Neurological Signs.

Case	Side of lesion	Cranial nerves							Horner's syndrome	Cerebellum	Spinal fillet
		V			VI	VII	VIII	X			
		Motor	Sensory	Descending							
1	R.	0	0	+	0	+	+	+	+	0	+
2	L.	0	0	+	0	+	0	+	+	0	+
3	L.	0	0	+	0	+	+	+	+	+	+
4	R.	0	0	0	0	+	+	+	+	0	+
5	R.	0	0	+	+	+	+	+	+	+	+
6	L.	+	+	+	+	+	+	+	+	+	+

From a study of Table II it is obvious that the lateral portion on the medulla is generally the site of these lesions and the structures located therein, namely, the nucleus ambiguus, spinal fillet, oculo-pupillary nucleus, facial nerve nucleus, and the descending tract and nucleus of the trigeminal nerve, suffer the greatest damage. More dorsolateral structures, as the nuclei of the eighth nerve and the cerebellar pathways (restiform body), are injured with any spread of the lesion.

These cases illustrate several points which are relevant to the anatomical physiology of the hind-brain. In all the cases in which there was subjective evidence of an involvement of the descending tract of the trigeminal nerve there was a subjective sensation of pain in that side of the face, which in some cases was quite severe. This pain was only transient in our cases, and as yet none have developed any severe trigeminal neuralgia such as that reported by Harris [12]. These cases illustrate the points emphasized by Spiller [14] in 1915, that the descending tract of the trigeminal nerve carries the pain and temperature sense from the face, and that the fibres in the descending tract cross at various levels and join the fibres carrying these types of sensation from the trunk. This last point is brought out in Cases 5 and 6, where the pain and temperature sensation on the contralateral side of the face was lost. The corneal reflex was lost on the side of the lesion in all of our cases, and this is in accord with Spiller's statement that the corneal reflex is connected with the fibres carrying the sensation of pain.

The disparity in the amount of dysarthria and dysphagia found in some of these cases is explained on the basis presented by Ramsbottom and Stopford [13]. They state that the upper portion of the nucleus ambiguus innervates the larynx and the vocal cords, while the lower portion of the nucleus innervates the muscles of the pharynx and the palate. In most of these cases the lesion can be placed fairly low in the medulla, and there was a marked dysphagia with only slight or moderate dysarthria, whereas in Case 6, in which the lesion extended high, there was extreme dysarthria and only slight dysphagia.

The Horner's syndrome is explained by involvement of the pupillary centre which is located by Combes [3] and others in the lateral reticular substance adjacent to the nucleus ambiguus and the descending tract of the trigeminal nerve. Its connection with the cervical centre is by the tractus intermedio-lateralis. It is also supposed to have a direct connection with the ciliary ganglion by fibres travelling up the descending tract of the trigeminal nerve and out of the brain-stem through the trigeminal nerve. Injury to these cells in the medulla result in a milder form of the Horner's syndrome than that found after a lesion of the cervical sympathetic.

Involvement of the spinal lemniscus was constant in these cases, and was accompanied by a subjective sensation of numbness on the contralateral half of the body; in two of the cases stimulation of the analgesic areas caused a perverted form of sensation somewhat similar to that occurring with injury to higher sensory centres, such as the thalamus.

The sense of taste was tested in only two of these cases, and in both (Cases 5 and 6) it was found to be absent on the homolateral half of the tongue. This is probably due to injury of the tractus solitarius.

The structures situated in the median portion of the medulla, i.e., twelfth-nerve nucleus, medial lemniscus and the pyramidal tract, are not involved in these cases, as they receive their blood supply through the anterior spinal artery. There was, however, in some of these cases, slight evidence of involvement of the pyramidal tract in the form of hyperactive reflexes, or abnormal plantar or abdominal reflexes on the side opposite to the lesion. This can probably be explained by œdema, &c. The diminution of deep reflexes which occasionally occurs in these cases (see Cases 4 and 6) has never been explained.

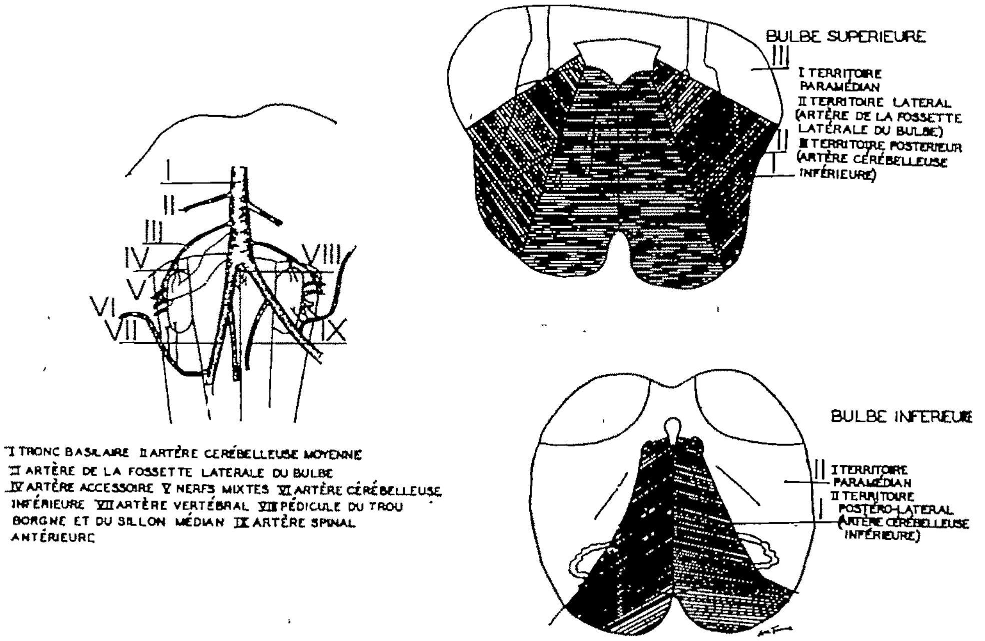
I
II
III
IV
V
VI
VII
VIII
IX
I TRONC BASILAIRE II ARTÈRE CERÉBELLEUSE MOYENNE
III ARTÈRE DE LA FOSSETTE LATERALE DU BULBE
IV ARTÈRE ACCESSOIRE V NERFS MIXTES VI ARTÈRE CÉRÉBELLEUSE
INFÉRIEURE VII ARTÈRE VERTÉBRAL VIII PÉDICULE DU TROU
BORGNE ET DU SILLON MÉDIAN IX ARTÈRE SPINAL
ANTÉRIEURE
BULBE SUPERIEURE
III
II
I
I TERRITOIRE PARAMÉDIAN
II TERRITOIRE LATERAL (ARTÈRE DE LA FOSSETTE LATÉRALE DU BULBE)
III TERRITOIRE POSTERIEUR (ARTÈRE CÉRÉBELLEUSE INFÉRIEURE)
BULBE INFERIEURE
II
I
I TERRITOIRE PARAMÉDIAN
II TERRITOIRE POSTÉRO-LATERAL (ARTÈRE CÉRÉBELLEUSE INFÉRIEURE)

FIG. 9.—Sketches showing the arrangement of the vascular supply to the hind-brain, and the areas of the hind-brain irrigated by each vessel.

Fig, 9 taken from Foix, Hillemand and Schalit [4], shows their conception of the vascular supply of the hind-brain, and it is their opinion that most of the so-called cases of thrombosis of the posterior inferior cerebellar artery are really due to a lesion of the artery of the lateral fissure.

Diagnosis.—The diagnosis of these cases is generally comparatively simple. The sudden onset of such a dramatic symptom as inability to swallow should lead to a consideration of a vascular lesion of the medulla, and in the differential diagnosis other causes of injury to the vagus nerve or its nucleus should be considered. The conditions which are most likely to give difficulty are tumours of the medulla, syringobulbia, and the rare cases of osteomyelitis of the temporal bone with involvement of the jugular foramen. The mode of onset and the absence of the concomitant findings of this syndrome, such as the Horner's syndrome, the involvement of the spinal lemniscus and the descending tract of the trigeminal nerve, are generally sufficient to exclude this syndrome. Dysphagia and dysarthria due to the loss of supranuclear control of the nucleus ambiguus, as occurs in pseudobulbar palsy, can easily be distinguished in the same manner.

Prognosis.—The prognosis in these cases, contrary to the current idea that vascular lesions in this situation are fatal, is very good. Though two of our cases died while in the hospital, in only one of the cases could the death be attributed to the vascular lesion, and in the eight cases reported by Riley [9] there were no fatalities. With the progress of time most of the symptoms and signs disappear or improve, with the exception of the sensory changes which are generally persistent.

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HÆMOPHILIA AS A CAUSE OF LESIONS IN THE NERVOUS SYSTEM.

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LESIONS in the central and peripheral nervous system are among the less common local manifestations of hæmophilia, yet they seem to occur often enough to merit consideration in neurological diagnosis. Occasionally the characteristic history of hæmophilia may not be volunteered by a patient, nor elicited by the clinician; and, as in the diagnosis and treatment of joint lesions, a serious mistake may be made through failure to bear in mind this possibility.

The classical memoir of Bulloch and Fildes [1] furnishes us with the most complete historical account of the disease. It contains the records of some nineteen cases in which lesions in the nervous system occurred spontaneously in hæmophiliacs; and it is certain that, in many of the cases, the disease itself was responsible. A summary of these cases follows:—

Mauthner, Max., 1863.—Epistaxis and apoplexy in a man aged 26.
Stromeyer, Louis, 1864.—Paralysis of great sciatic nerve.
Tamele, J., 1869.—Cerebral hæmorrhage.
Traneus, L., 1870.—Ventricular hæmorrhage in a child.
Grandidier, 1872.—Subarachnoid hæmorrhage (Schulz's case).
Lemoine, 1874.—Cerebral hæmorrhage.
de Rute, F., 1884.—Cerebral hemorrhage.
Sarra, R., 1890.—Subarachnoid hæmorrhage in a baby.
Berggrun, Emil, 1896.—Cerebral hæmorrhage.
Pearson, H. B. A., 1904.—Cerebral hæmorrhage.

Family Histories:—

Gocht's case, IV 4.—Subdural hæmorrhage.
Ledoux's case, IV 2.—Hæmatomyelia.
Wright's case 2, III 24, "Edwin."—Cerebral hæmorrhage.
Miles' case, III 2.—Hæmorrhage in the cauda equina.
Bjørkman and Liedbeck's case, II 2.—Hæmorrhage round the pons Varolii, the optic nerves, and the right cerebellar hemisphere.
Van der Scheer's case, 2.—Massive fatal hæmorrhage into the spinal canal.
Forster's case, 2, IV 5.—Meningeal hæmorrhage.
Cousins' case, II 2.—Blood extravasation at the base of the brain.
Getting's case, VI 50.—Lower limb "partially paralysed."

Since 1911, only one case of damage to a nerve due to hæmophilia has been described. J. B. Lord, of Omaha, has given an excellent account of a spontaneous hæmorrhage occurring in a hæmophilic boy, causing ulnar nerve palsy and ischæmic contracture of the muscles of the forearm [2]. A most comprehensive German work on hæmophilia that appeared recently contains no references to lesions in the nervous system [3].

In an attempt to estimate the relative frequency of such lesions, I have examined the records of two large hospitals. In one (St. Bartholomew's Hospital, London) nineteen cases of hæmophilia were admitted to the wards over a period of twenty-three years; in the other (University Hospital, Ann Arbor, Michigan, U.S.A.) ten cases were admitted over a period of fourteen years. The various lesions occurring in these twenty-nine cases are listed below :

	Number	Percentage
Total number of cases	29	100
Epistaxis, bleeding from teeth, minor injuries	29	100
Hæmarthroses (generally multiple and recurrent)	24	82·8
Hæmatemesis and melæna	9	31·0
Hæmaturia	8	27·6
Hæmorrhage into the eye	1	3·6
Hæmorrhages causing nervous lesions	2	7·2

This table brings out two interesting points : first, that of the major lesions, hæmarthrosis is by far the most common; and, second, that lesions in the nervous system are rare events in the life of the hæmophiliac.

CASE RECORDS.

Two cases are described; the first was studied in the Orthopædic Department of the University Hospital, Ann Arbor, Michigan, U.S.A.; the second at the Royal National Orthopædic Hospital, London. The second patient was presented at a clinical meeting of the Neurological Section of the Royal Society of Medicine in November, 1929 [4].

Case 1.—R. H., male, aged 22, labourer.

History.—September, 1928. The patient first complained of soreness followed by numbness in the right groin and the anterior surface of the thigh. The right lower extremity became weak, and some difficulty in walking was experienced. Ten days after the onset of symptoms, a swelling appeared in the right lower abdomen; it was almost painless, but gradually increased in size.

Family history.—Apparently the patient's brother is the only other member of the family with any tendency to bleed spontaneously. No details are given from which one might make a positive diagnosis of hæmophilia in the brother.

Past history.—When aged 10, he had great trouble with epistaxis and bleeding after the extraction of teeth.

When aged 17 his left lower extremity swelled and was painful for two weeks. Later, it was noticed that the limb was shorter than the right, and the patient believes that the hip-joint was a little stiff. The lesion was regarded as tuberculous by his doctor, who ordered him to bed for four months. After this treatment the patient got about quite comfortably, though at first he found it necessary to use crutches.

On examination.—Joints: Left hip, no fixed deformity, active flexion possible to 100°, all other movements very limited.

Right hip, 35° limitation of extension due to contraction of the psoas.

Spine: slight increase in the lumbar lordosis, secondary to the psoas contraction.

Nervous system (all physical signs on the right side).—Sensory: anæsthesia over the areas of distribution of the middle and internal cutaneous nerves of the thigh and the long saphenous nerve.

Motor: no contraction elicited voluntarily or by electrical stimulation in the rectus femoris, vastus externus, vastus internus, crureus, pectineus or sartorius. Complete inability to extend the knee voluntarily.

Abdomen: in the right lower quadrant, lying in the hollow of the ilium, was a mass extending almost to the midline and causing a little bulging in the loin. It was elastic in consistency, had a smooth surface and was not tender.

X-ray examination of the spine was negative. Films of the hip-joints showed considerable destruction of the head of the left femur, and some bony proliferation along the roof of the acetabulum and the margin of the femoral head.

Coagulation time of the blood was ten minutes.

Subsequent history.—By July, 1929, the anterior muscles of the thigh were contracting well; all numbness had disappeared. The patient still walked with a slight limp. The abdominal swelling had disappeared.

On the findings enumerated above, a diagnosis was made of hæmophilia, complicated by hæmorrhage involving the left hip-joint and a right ilio-psoas hæmatoma pressing on the femoral nerve.

There must be an element of doubt in the first part of the diagnosis. The absence of a characteristic family history and the relatively short clotting time of the blood do not suggest classical hæmophilia.

Case 2.—S. L., male, aged 24, chauffeur.

History.—June 9, 1928. The patient was involved in a motor car accident and was admitted to hospital. He was unconscious for three days as the result of "concussion." A radiogram of the spine was said to show a fracture in the region of the third and fourth lumbar vertebræ; there was some injury to the right ankle, but apparently no bony lesion. He remained on his back for four months, and returned to work six months after the accident, not wearing any form of spinal support. At this time the patient noticed that he occasionally lost control of his legs and fell. There was no actual paralysis and no loss of consciousness.

Early in 1929, he stumbled and injured his right hip. A large swelling appeared in the upper and outer part of the thigh; X-ray examination did not show any fracture of the femur. The swelling gradually disappeared.

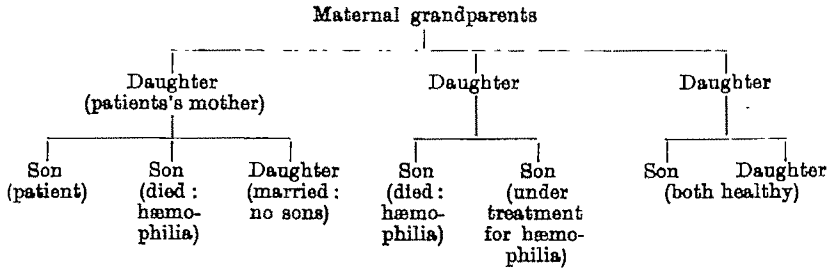
In May, 1929, his right ankle gave way, and he was admitted to hospital with a large swelling of the joint, but again no fracture.

In June, 1929, after a drive of 120 miles (without accident), the patient became aware of a sudden weakness in the left lower limb. There was an almost instantaneous paralysis of the muscles extending the left knee. He experienced a severe boring pain in the left loin, radiating down the left lower limb. This persisted for ten days.

September, 1929, "pins and needles" were sometimes felt in the right lower limb but no muscular weakness.

Micturition was normal and the bowels were kept regular by medicine.

Family history.—The history of hæmophilia is summarized below :—



Past history.—In 1926 the patient was admitted to hospital on account of severe hæmaturia and remained there for six months. There were no marked constitutional signs.

On examination.—Nervous system. Sensory: An area in the left lower limb corresponding fairly closely to the distribution of the anterior divisions of the third and fourth lumbar nerves was insensitive to cotton-wool, pin-prick and differences of temperature. Vibrations of tuning fork were not felt on the left patella, and only felt poorly at the upper and lower ends of the fibula. General diminution in tactile sensibility in the whole of the left lower limb. Joint sensibility everywhere normal.

Reflexes: Biceps, triceps, supinator and ankle-jerks strong and equal on both sides. Right knee-jerk easily obtained, left absent. Abdominal and cremasteric reflexes normal. Plantar reflexes flexor.

Motor: No contraction elicited in left quadriceps extensor muscle, pectineus and adductor magnus. The adductor longus and tensor fasciæ femoris contracted strongly. There was slight wasting of the gluteus maximus.

Recent skiagrams showed no abnormality of the spine.

Lumbar puncture was not performed on account of the blood condition.

The urine was normal.

Clotting time of the blood well over one hour and forty minutes.

When last seen (in December 1929) there was no appreciable alteration in the patient's condition.

Only those muscles supplied exclusively by fibres from the third and fourth lumbar segments were completely paralysed; the sensory loss corresponded to the cutaneous areas for the same segments. It seemed reasonable, therefore, to make a diagnosis of hæmatomyelia at the level of the third and fourth lumbar segments. Probably the injury to the spine in June, 1928, prepared the way for the hæmorrhage.

SUMMARY.

(1) Hæmophilia is occasionally responsible for lesions in the nervous system.

(2) Central lesions are more common than peripheral.

(3) The condition is worth bearing in mind in neurological diagnosis.

(4) Two cases are recorded.

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THE INFLUENCE OF EXPERIMENTAL LESIONS OF THE SPINAL CORD UPON THE KNEE-JERK. I.—ACUTE LESIONS.[1]

BY J. F. FULTON, E. G. T. LIDDELL, AND D. McK. RIOCH.

(*From the Laboratory of Physiology, Oxford.*)

[The expenses of this research were defrayed in part by a grant from the Medical Research Council.]

When Ballif, Fulton and Liddell [1] communicated their paper on the differences between "spinal" and "decerebrate" knee-jerks to the Royal Society, the late Sir David Ferrier asked what descending tracts in the spinal cord were responsible for the differences which had been described. The question could not then be answered, and as it has since remained unanswered we have undertaken to investigate the problem and venture now to record our findings. Ballif and his co-workers [1] observed that the knee-jerk of a decerebrate preparation is briefer and always much more difficult to inhibit by a single break-shock stimulus than the jerk of the same preparation after transection of the spinal cord in the dorsal region. This indicates that the "higher centres" exert an influence which tends to abbreviate the jerk and to protect it from inhibition. Denny-Brown [8, 7] has shown that in a muscle composed of mixed fibres, as is the knee extensor, the briefer duration of the "decerebrate" jerk is due to the more ready participation of rapid muscle fibres ("white"). The rapid "white" fibres are inactivated by the spinal severance and thereafter the slower "red"[2] fibres become prominently active. The descending nerve paths responsible for these differences cannot be any of those arising above the level of the colliculi, for the brain-stem had been transected at the mid-collicular level. If transected just posterior to the posterior colliculus so as completely to exclude the red nucleus the result is still the same. Consequently the descending fibres in which we are interested are not those in the rubrospinal tract, and they must therefore arise in some centre caudal to the posterior colliculus.

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[1] Part II reporting fibre degenerations and myographic findings three weeks after surgical lesions of the spinal cord will be published later. A preliminary note has appeared in the *Journal of Physiology* (1930, 69, Proc., xxvii-xxviii).

[2] We have used inverted commas since Dr. Denny-Brown [8] was careful to point out that while red fibres are often slow, "redness" in itself does not necessarily imply slowness of contraction.

The history of the study of experimental lesions of the spinal cord has been described by Sherrington [31] with special reference to the results of lateral semisection, and by Page May [22] who dealt with experimental lesions in relation to the sensory pathways in the cord. Both authors give full bibliographies of early literature. It will be remembered that Brown-Séquard [2, 3], from an experimental study of semisections carried out between 1847 and 1855, was the first to insist upon the early crossing of fibres conducting pain after their entry into the cord, and upon the uncrossed situation of motor weakness following such lesions. Some of his views were erroneously opposed by Schiff [27] who, however, was among the first to study the consequences of lesions restricted to individual pathways such as the posterior columns. An elaborate series of semisections was reported from Goltz's laboratory in 1882, by Osawa [24], and he it was who described the remarkable fact that two semisections on opposite sides of the cord, if separated by a space of six segments from one another, are followed, after a long interval, by sufficient return of voluntary power to enable the animal to use its hind limbs (somewhat falteringly) for the purpose of progression. In one experiment three semisections were successfully carried out and although all sensation was permanently abolished the animal was eventually able to stand. A series of beautifully circumscribed semisections (monkeys) were reported in 1892 by Mott [23] who drew the important conclusion that whereas pain was diminished below the level of semisection on the opposite side of the body, position sense and touch were lost on the same side. Though certain of Mott's further interpretations have not been substantiated, his conclusions concerning homolaterality of position sense have been amply confirmed. A further series of semisections in monkeys was published by Turner [38]. Gotch and Horsley [16] in the same year studied the effects of acute lesions of the spinal cord upon various reflexes, but the knee-jerk was not analysed. The later studies of Lewandowsky [18], Rothmann [26], Page May [22], and others, in which various quadrants and sensory areas were cut with a view to studying sensory pathways, have proved to have little immediate bearing upon the problem which we now propose to consider. Their work on sensation is fully treated by Head [17], and we do not intend in this paper to deal with literature of the sensory pathways or to consider, except incidentally, the sensory disturbances which our operated animals showed.

METHOD.

A series of nineteen cats was used in the investigation recorded in Part I of this paper. All animals were decerebrated by the trephine method under profound ether-chloroform anæsthesia. In some preparations (used in conjunction with the study of another problem) the level of transection was well precollicular. When acute lesions were to be made the spinal cord was exposed at a suitable level under anæsthesia, prior to decerebration. After decerebration spinal lesions were made without anæsthesia. The hind-limbs were completely immobilized on both sides by appropriate nerve section or tendon resections, excluding only the nerves to the two quadriceps muscles under examination. Both patellar tendons were isolated, and the preparation securely fixated on both sides to the experimental table so that first one and then the other tendon could be examined by a slight shift of the table. During the first part of the research a torsion-wire myograph of the old pattern was used [33, 34, 15], but the larger number of observations have been made with a new frictionless myograph [5, 12]. It consists of a flat steel strip tightly clamped at both ends and under tension longitudinally. The lever arm is mounted in the middle of the strip, and its excursion is rectilinear, without distortion up to a tension of 6 kg. Its natural vibration frequency is 960 d.v. per sec. Electrical responses have been obtained simultaneously with the mechanical responses [15, 6, 7 &c.] by means of an Einthoven galvanometer. The tendon was tapped two to three times a second by an insulated metal rod held in the hand. Inhibitory stimuli consisted of single break-shocks from a coreless Berne coil, which throughout the whole series of experiments remained at 3 cm., i.e., a strong stimulus, well over maximal for every preparation. When applied to a motor nerve, however, there was no evidence that a stimulus of this intensity ever produced more than one volley of nerve impulses. The peroneal nerve has been used in most instances, and the electrodes were of the Sherrington shielded type. All records were photographic, the technique employed being that previously described in other investigations published from this laboratory [33, 34, 1, 5, 15, &c.]. The spinal cord was removed at the end of the experiment fixed for a week or more in 5 per cent. formalin, and the extent of the lesion examined in thin macroscopic sections.

I.—*Lateral Semisection of the Spinal Cord* (*low dorsal*).

If a single strong break-induction shock is applied to a nerve of the hind-limb from which a series of knee-jerks is being elicited, e.g., at

3 per second, one jerk may be completely inhibited, provided that the inhibitory stimulus occurs at a brief interval before the jerk (fig. 1). In the decerebrate condition the extensor centres recover within 20 to 30 σ from the inhibition so induced, but when the preparation is made "spinal" as much as 3 seconds may be required before complete recovery [1]. We have therefore used this feature of the difference between the spinal and decerebrate state for the analysis of the pathways. By taking successive observations with intervals at random, curves can be drawn representing the rate of recovery of the spinal centre from the stimulus (fig. 2). Analysis therefore has consisted in plotting the curves of recovery after any given lesion. We have also studied the duration of the jerk, but as this feature is somewhat more difficult to analyse and to represent graphically it has not been employed. In general, however, it may be said that when the knee-jerk is highly susceptible to inhibition only the more slowly contracting fibres ("red") in the muscle appear to respond [7, 8].

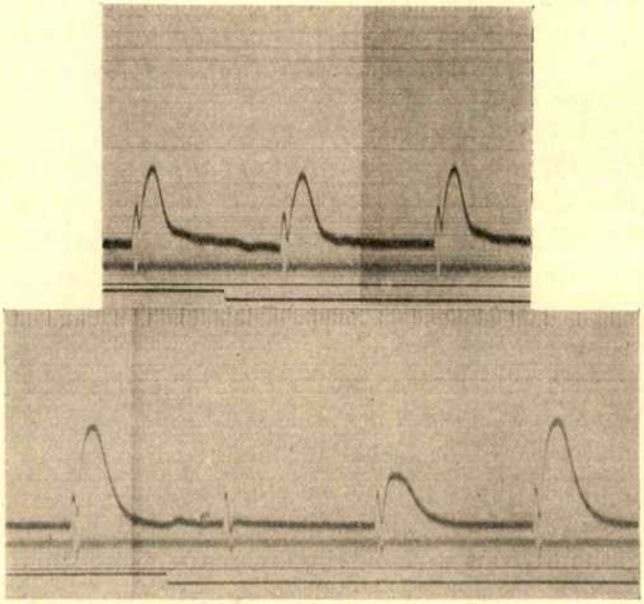

FIG. 1.—Simultaneous electrical and mechanical records of knee-jerks. The taps are seen in the myogram as initial upstrokes preceding the response. An inhibitory break-shock is applied to the peroneal nerve at the fall of the signal at bottom of record. Galvanometer string is between myograph and signal. Time at top of record = 0·02 sec. Upper record: Vasto-crureus in decerebrate cat. Lower record: Same muscle after making a small lesion in ventral quadrant of spinal cord on the side of the muscle in lower thoracic region. This lesion produces a characteristic "spinal" state.

In order to study the effects of incomplete lesions of the spinal cord it is essential first to analyse the results of complete semisection. If the knee-jerks are examined after an acute semisection, the jerk on the divided side is indistinguishable from the jerk of a preparation in which total transection has been made, while on the uninjured side the jerk remains typically "decerebrate" in all its features. Thus, in Experiment XXI, a precollicular preparation, the knee-jerk was of brief duration and could not be inhibited unless the break-shock fell within 20 σ of the tap. The spinal cord was semisected on the right side, and the jerks on the left still remained "decerebrate" in character, indicating that the descending tracts on the opposite side do not exert an appreciable influence. (Same result obtained in Experiment VII.) An ipsilateral "semisection" was then performed, after which the jerks became typically "spinal" in character. The curves of recovery before and after these two procedures are indicated in fig. 2, together with diagrams showing the extent of the lesion. It will be seen that after the "semisection" a single shock to a nerve on the same side served completely to inhibit the jerk on that side for 300σ, and a state of partial inhibition continued for 2 seconds. A subsequent complete transection in this experiment caused no increase in the susceptibility to inhibition. We gained similar results in five other preparations.

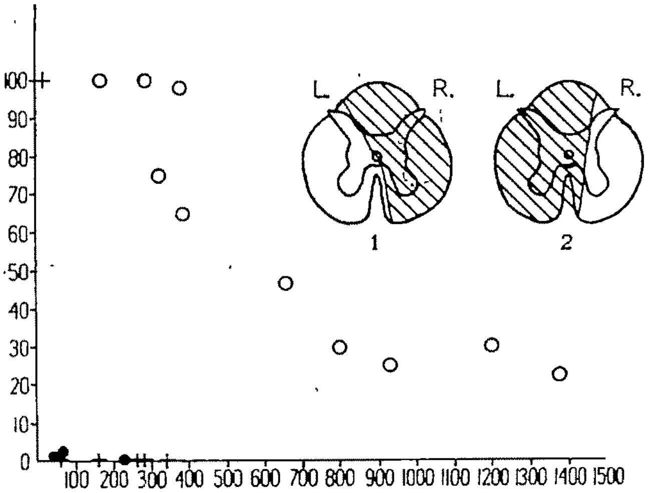

FIG. 2.—Left vasto-crureus. Recovery curve of the knee-jerk after a single inhibitory break-shock to peroneal nerve. Ordinates = degree of inhibitory depression of response expressed as percentage of a normal response to a series of equal taps. Abscissæ = time in sigmata after inhibition. Extent of partial spinal lesion shown diagrammatically. + Before any lesion. ● After right "semisection." O After left "semisection."

In some experiments both quadriceps muscles were prepared. On semisection at D.13 the knee-jerk on the same side became immediately "spinal" in character, while that on the opposite side remained "decerebrate." They became indistinguishable from one another after complete transection. In three instances complete transection at mid-dorsal level has been followed by moderate increase in the susceptibility to inhibition on the previously divided side, which suggests that the integrity of the spinal cord on the opposite side may serve to diminish slightly the susceptibility to inhibition (this has also been seen in some experiments in which the cord has been cut aseptically some days before). In Experiment XIX, for example, three distinct curves of recovery from inhibition are seen: (*a*) with the spinal cord intact; (*b*) after ipsilateral semisection at a low dorsal level; (*c*) after complete transection at a low dorsal level (fig. 3). In only one instance has a contralateral semisection noticeably influenced the jerk; in this case, however, the influence was slight, and may possibly have been due to local œdema set up by the operation (Experiment XII).

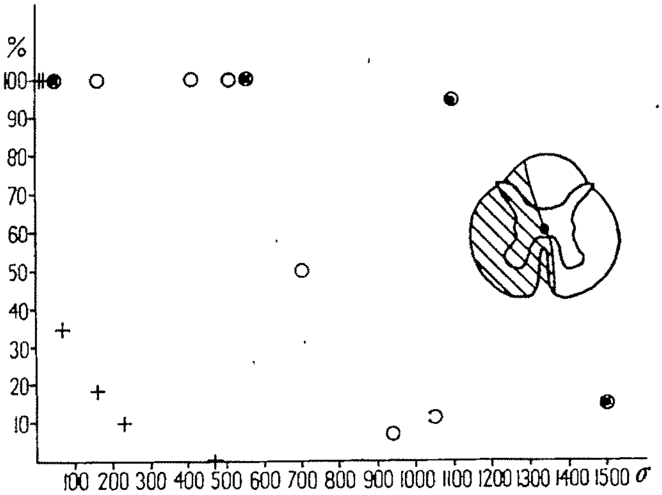

FIG. 3.—Left vasto-crureus. Ordinates and abscissæ as in fig. 2. Extent of left "semisection" shown diagrammatically. + Before spinal lesion. ○ After left "semisection." ⊙ After complete transection.

II.—*Partial Lesions* (*other than Semisections*).

Since a semisection of the spinal cord serves to make the knee jerk on the same side "spinal" in character, we were led to consider the results of incomplete semisections. Those performed acutely were found of significance only when the inhibitability of the knee-jerk remained unchanged. When it became "spinal" in character the result might be due to local œdema or to direct trauma affecting the unsevered parts of the cord. Difficulties of interpretation arising from this source are not present in chronic lesions, for the œdema usually passes off, and the extent of the primary lesion can be judged by the resulting degenerations. There are, however, other complicating factors in the chronic preparations, especially the inevitable compensation which occurs [31, 35, 36]. We are therefore inclined to place significance upon the results of acute lesions.

In each of a series of ten animals, one or more partial transections have been made, and the effect of each lesion on the knee-jerks has been carefully analysed. We propose to enumerate these with diagrams in the order in which they were performed.

Experiment II.—Precollicular preparation; right quadriceps recording, giving at first normal "decerebrate" jerks, difficult to inhibit. After a lesion which subsequently was found to involve the dorsal two-thirds of the spinal cord on both sides at D.10, there was no change in the duration of the jerk (90σ), and the inhibitability was only slightly increased. The extent of the lesion is shown diagrammatically in fig. 4. After complete transection of the cord the jerks increased in magnitude (4 mm. to 19 mm.) and duration (90 to 160σ) and the inhibitability of the jerk was increased more than twofold.

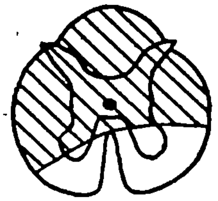

FIG. 4.—Description in text.

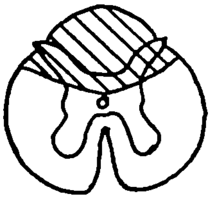

FIG. 5.—Description in text.

Experiment III.—Precollicular preparation; right quadriceps recording with normal "decerebrate" jerks. A lesion at D.9 affecting the posterior columns on both sides, the dorsal part of both lateral columns and extending downward as far as the central canal (fig. 5) had no effect on the inhibition or on the duration of the jerk. Dial was given to this preparation intraperitoneally (0·5 c.c. per kilo) and it served only to make the knee-jerk more difficult to inhibit. The spinal cord was not transected.

Experiment IV.—A precollicular preparation; right quadriceps recording giving characteristic, brief "decerebrate" jerks difficult to inhibit. At intervals of 30 to 40 minutes three lesions were made at levels ranging from D.7 to D.10

(see fig. 6), the first in the upper third of the right dorsal quadrant; the second was a stab wound affecting a triangular area involving the grey matter and posterior columns; and the third an extensive lesion involving the whole left side of the cord and the right dorsal quadrant. These three lesions were each without any recognizable effect upon the duration (60σ) or the inhibitability of the jerk. Ten minutes after complete transection the duration of the jerk had risen to 180σ and the recovery curve from inhibition had become characteristically prolonged.

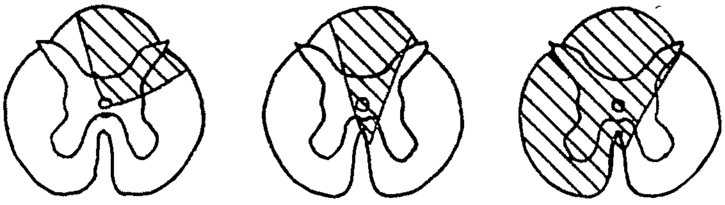

FIG. 6.—Description in text.

It is quite clear then from these three preliminary experiments that pathways controlling the extensor centres pass downwards in the ventral quadrant of the spinal cord and do not cross below the level of our lesions. Subsequent efforts to localize these tracts more accurately have been suggestive but not conclusive. Acute experiments have been somewhat variable, possibly because of trauma incident to the transection and probably also because the descending tracts are scattered diffusely through the ventral quadrant of the cord. The next experiment suggests that the descending tracts are perhaps not sharply circumscribed.

Experiment V.—Midcollicular preparation with good decerebrate rigidity; right quadriceps recording and yielding brief "decerebrate" jerks difficult to inhibit. An extensive lesion (fig. 7, No. 1) involving the dorsal two-thirds of the right half of the spinal cord was followed by considerable increase in susceptibility to inhibition. Subsequent complete semisection (fig. 7, No. 2) had little further effect, but complete transection increased susceptibility to inhibition on the right side by 20 per cent. to 30 per cent. It is likely that this experiment had been complicated by local œdema.

Having found that the dorsal quadrant of the spinal cord could be transected rostral to the extensor centres of the hind-limb without influencing the jerk, we next attempted to produce localized lesions of the ventral quadrant of the cord in order to learn whether they would influence the jerk when the rest of the cord remained intact. Lesions of the ventral quadrant are difficult to place accurately since the approach to the cord is from the dorsal surface. In successful instances it has appeared evident that circumscribed destruction of this area of the spinal cord does in fact cause a "decerebrate" jerk to become "spinal" (fig. 1). For the reason mentioned at the beginning of this section positive evidence drawn from acute lesions is, however, less satisfactory than negative evidence. Two representative experiments will be described, in the first of which the evidence is positive, in the second significantly negative.

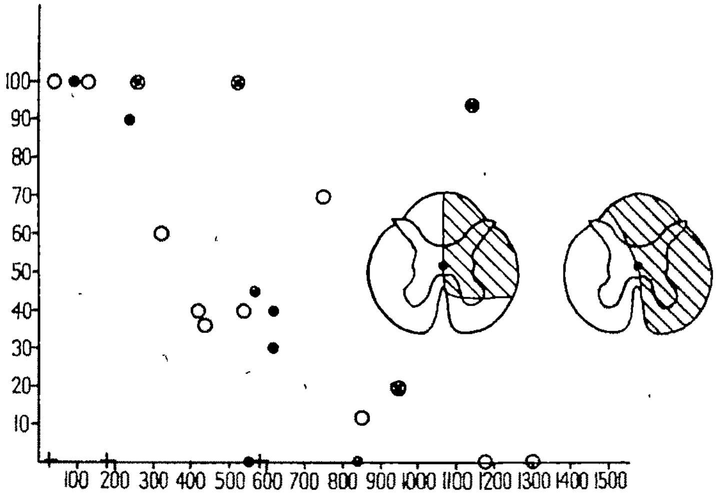

FIG. 7.—Right vasto-crureus. Ordinates and abscissæ as in fig. 2. + Before spinal lesion. ● After section of right dorsal quadrant lesion (1). ○ After semisection, lesion (2). ⊙ After complete transection.

Experiment XIII.—Precollicular preparation; left quadriceps recording. Before any lesions of the cord were made the curve representing the recovery from inhibition of the jerk was characteristic of that of a precollicular preparation. After an extensive lesion restricted to the right ventral quadrant of the spinal cord at D.9, there was no increase in the susceptibility to inhibition of the jerk, the curve being that usually seen in a typical decerebrate preparation (fig. 8). After a second lesion, this time restricted to the left ventral quadrant (at D.10), the knee-jerks on the left side became typically "spinal" in character, becoming enhanced in duration from 60σ to 90σ, and showing a recovery cure in which the size of the jerk was still 50 per cent. below normal one second after a single inhibitory stimulus. On subsequent complete transection of the cord at D.8 the recovery curve of inhibition and the duration of the jerk were not changed significantly.

This experiment indicates that a lesion confined to the ventral quadrant on the same side as the jerk serves to make it "spinal" in character.

The next experiment was similar, only it so happened that the second lesion was incomplete, failing to extend to the midline. The conclusion to be drawn was that the nerve-fibres with which we were concerned passed downwards in a medial sector of the ventral quadrant.

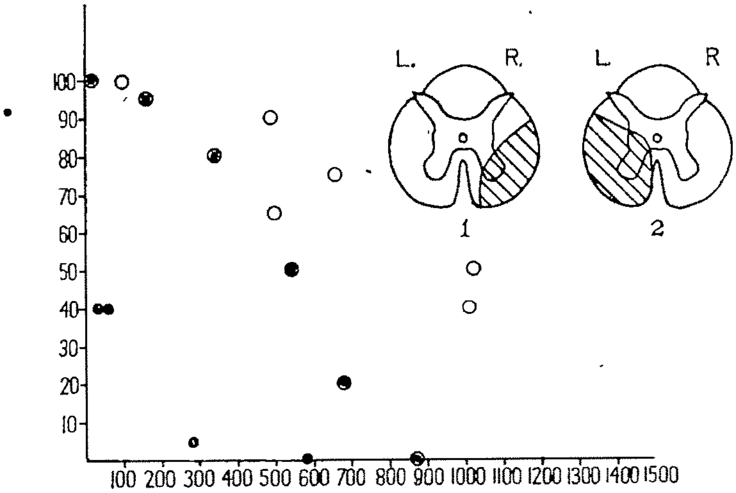

FIG. 8.—Left vasto-crureus. ● After right ventral quadrant lesion (1). ○ After left ventral quadrant lesion (2). ⊙ After complete transection.

Experiment XVIII.—Precollicular preparation; left quadriceps recording. Before a lesion of the cord had been made, recovery from a single shock was complete after 50 to 100σ. This was also true after a large lesion of the right ventral quadrant extending to the midline. After a lesion of the left ventral quadrant which extended to within about 1 mm. of the midline there was still no change in the recovery curve from inhibition. After the cord had been completely transected, however, the characteristic "spinal" curve resulted and the duration of the jerk became increased from 60 to 140σ.

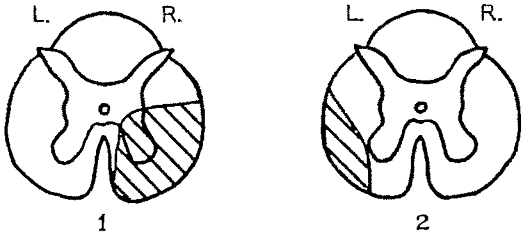

FIG. 9.—Description in text.

Acute experiments then point definitely in one direction; namely, that the fibres responsible for the "decerebrate" characteristics of the jerk pass downwards in a medial sector of the ventral quadrant in an area which would include the vestibulospinal pathway. When this region is cut not only does the jerk become spinal in character but the crossed extensor reflex disappears. Further observations, derived from the study of "chronic" preparations, will be reported later.

III.—*The Influence on the Knee-jerk and Stretch Reflex of Transection of the Cord caudal to the Segments supplying M. quadriceps.*

An observation long familiar to those who have worked with decerebrate preparations is that on transection of the spinal cord in the dorsal region the decerebrate rigidity of the fore-limbs becomes very greatly augmented. The effect is a lasting one, being seen a few minutes after transection and continuing some days after decerebration. It would appear that the centres of the fore-limbs are inhibited normally by impulses ascending from the hind-limbs, and that transection of the cord serves to release them. In analysing this effect more in detail, Denny-Brown and Liddell [9, pp. 362-363] found that the stretch reflex of M. Supraspinatus is greatly increased by post-brachial severance of the spinal cord, and they draw attention to Sherrington's and Lazlett's [36] observations that the direct "spino-cerebellar" tract becomes diminished in size as it ascends the spinal cord. Undoubtedly there are also other tracts which transmit influence from the more caudal segments. Fröhlich and Sherrington [14], for example, found that stimulation of the transverse cut surface of the spinal cord in the lumbar region with stigmatic electrodes caused inhibition of decerebrate rigidity in the fore-limbs when a circumscribed area just lateral to the ventral horn was stimulated. Changes in position of the hind-limbs produce alterations in the posture of the fore-limbs [25].

These observations suggested that even in the case of the hind-limb the more caudal segments of the cord might exert an inhibitory influence upon the rostral extensor centres; and that, for example, transection of the cord at the sixth or seventh post-thoracic level might diminish the susceptibility to inhibition of the "spinal" jerk. In 1893 Sherrington had observed [19] that "the briskness of the 'jerk' may in like manner be increased by section in the spinal canal of the spinal roots, either sensory or motor, adjacent to that one most intimately concerned with the jerk, and especially of the muscular nerves to the antagonist of the 'jerk's' muscles," but transection of the cord was not examined in these experiments. Our procedure has been to examine first the jerks in an ordinary decerebrate preparation, after which the spinal cord has been transected in the dorsal region and the jerks and their inhibition again examined. Soon after spinal transection and for about twenty-four hours subsequently, it is usually impossible in the cat to obtain a stretch reflex (this being one of the prominent manifestations of spinal shock). Having found the stretch reflex to be absent, the spinal cord has then been transected at some level caudal to L.5.

In one experiment (XXXVI) in which the cord was transected between L.5 and L.6 all of the nerves from muscles antagonistic to quadriceps being thus excluded, one of the prominent symptoms of spinal shock, i.e., the absence of stretch reflex, disappeared. We were not able in this experiment to test the susceptibility of inhibition since the chief afferent pathways had been cut. In the following experiment the transection was made between L.6 and L.7 so that one, at least, of the large caudal segments from which the sciatic nerve arises was left intact.

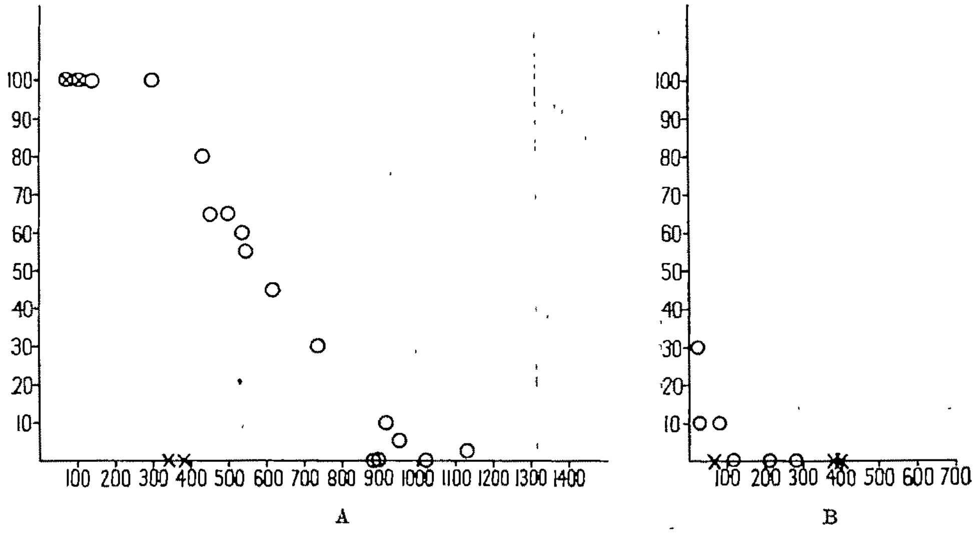

FIG. 10A.—Right vasto-crureus. O After right semisection at L 1. X After complete transection at L.6.

FIG. 10B.—Same preparation. Left vasto-crureus. O After right semisection at L.1. X After complete transection at L.6.

Experiment XXXVII.—Midcollicular preparation with right semisection at L.1 before observations were made. The recovery curve of the right quadriceps was "spinal" in character, while on the left it was typically "decerebrate" (fig. 10, A and B). The spinal cord was then transected between L.6 and L.7, after which there was a very marked increase in the briskness of the jerk on the right side with reappearance of stretch reflex, and the recovery curve had moved to the left of the chart (fig. 10A). Before the lower lumbar transection recovery on the right had not been complete until 900 to 1000σ, whereas after the transection recovery was complete after 340σ.

Though it is difficult to exclude altogether the possibility that the result is due to a diminution in the total number of effective fibres from the afferent nerve used for stimulation, it is improbable that this would account entirely for the result, since it is well known that a small nerve may be quite as effective in producing inhibition as a large one. The result, therefore, suggests that transection of the spinal cord caudally affects the three major symptoms of spinal shock: (1) susceptibility to inhibition; (2) the stretch reflex; (3) the crossed extensor reflex (see Part II).

Similar observations have been made in four other experiments with minor modifications of procedure. We have found in addition that section of the cauda equina at the tenth post-thoracic level is without influence upon spinal shock. Similarly, section of the left posterior roots L.7 and L.8 had no demonstrable influence upon the knee-jerks of the right quadriceps. Transection of the cord at the eighth post-thoracic level appeared to exert a slight influence. From these observations it appears to us that a transection of the cord which removes the influence of the antagonist tends very markedly to diminish the symptoms of spinal shock in the quadriceps.

DISCUSSION.

Our observations offer two points of interest to the clinical observer: (1) That "spinal shock," so-called, in so far as it affects the knee extensor, is a condition associated with a very marked increase in the susceptibility to inhibition, as judged by the knee-jerk and the crossed extensor reflex; and (2) that this "spinal shock," in the cat at least, does not develop until the descending pathways in the ventral quadrant of the spinal cord have been disturbed. It appears, also, that the more important pathways descend in a medial sector of the ventral quadrant in a region which would include the vestibulospinal tracts. So long as these are intact the limbs retain their extensor posture, and the knee-jerk is brisk, brief and difficult to inhibit. We have a few observations which suggest that the neck and labrynthine reflexes still exert their effect upon the knee-extensor. The observations are in harmony with those made by Cairns and Fulton [4], who found when radon was applied to the spinal cord (in a dose of 5 millicuries or greater) that the animals passed through a stage of marked hyperextension of the hind-limbs, lasting sometimes as long as twenty-four hours, before passing into a flaccid paraplegia. In one of their animals which remained permanently in extension on one side, the descending pathways in the medial sector of the ventral quadrant on that side had been spared. In such preparations the scratch reflex is still elicitable from stimulation behind the ear, which is in harmony with the observations of Sherrington and Laslett [35]. In his studies of tonus of skeletal muscle Spiegel [37] found that lesions of the ventral cord produced a marked and long-continued hypotonus of the skeletal musculature on the same side, whereas lesions of the lateral and dorsal columns produce only a slight and transient hypotonus of the homolateral musculature.

The fact that the vestibulospinal pathways appear to be responsible for the differences between the "decerebrate" and "spinal" jerk is in harmony with the experiments of Magnus [21, p. 434; see also 15, p. 530], that decerebrate rigidity continues to exist so long as the transection of the brain-stem does not injure the vestibular nuclei, i.e., it must fall somewhere between the anterior colliculus and the level of the vestibular nuclei. Immediately the vestibular nucleus is excluded decerebrate rigidity vanishes. If pathways other than vestibulospinal are concerned in causing the difference between the spinal and the decerebrate condition, they must arise at or caudal to the vestibular area.

Our conclusion is that spinal shock is characterized by the more or less permanent existence within the spinal cord of increased susceptibility to inhibition from external stimuli. Whether this is due to an intrinsic increase of the central inhibitory state of all or certain neurones, or to an intrinsic decrease of their central excitatory state, is a problem which awaits investigation.

SUMMARY.

(1) One of the major physiological symptoms of spinal shock is an increased susceptibility to inhibition. The knee-jerk, for example, may be inhibited for a period of several seconds by applying a single break-induction shock to a sensory nerve of the hind-limb. In the intact animal, or in a decerebrate preparation, it is exceedingly difficult and often impossible to inhibit a knee-jerk by a corresponding stimulus. The present paper records a series of experiments in which the attempt was made to determine the pathways responsible for the differences between the decerebrate and spinal condition, as judged by the inhibition of the knee-jerk.

(2) Acute lesions were made at levels ranging from D.8 to L.1, after which knee-jerks were examined by means of a frictionless torsion-wire myograph of high natural vibration frequency, with simultaneous registration of the electrical response according to the technique described by Ballif, Fulton and Liddell.

(3) Complete lateral semisection of the spinal cord causes the knee-jerk on the side of the semisection to assume "spinal" characteristics, while the jerk on the opposite side remains "decerebrate."

(4) The dorsal two-thirds of the spinal cord may be cut through without causing the knee-jerk to become "spinal" in type on either side.

(5) In acute preparations isolated transections of the ventral quadrant of the spinal cord on one side cause the knee-jerk on the same side to become "spinal."

(6) We conclude from these observations that the descending pathways responsible for the differences between the "decerebrate" and "spinal" conditions pass in the ventral quadrant of the spinal cord, probably in the medial half. The vestibulospinal tracts therefore suggest themselves since they are the most important descending fibres in this area.

(7) Transection of the spinal cord caudal to the knee-jerk centres causes great enhancement in their activity, diminution in susceptibility to inhibition, and, in a "spinal" preparation, the prompt reappearance of the stretch reflex.

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THE INFLUENCE OF UNILATERAL DESTRUCTION OF THE VESTIBULAR NUCLEI UPON POSTURE AND THE KNEE-JERK.[1]

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IT has been known for many years that the level of the brain-stem corresponding with the vestibular nuclei is essential for the maintenance of decerebrate rigidity [14, 16, 3, 10, 12], but precise information concerning the source and nature of the influence exerted by this area upon the spinal cord is lacking. In a previous communication [4] we pointed out that decerebrate rigidity continued to exist as long as the ventral quadrant of the spinal cord on the same side remained intact, and that when this area was destroyed reactions below the level of the lesion became spinal in character, even though the opposite lateral half of the spinal cord was uninjured. Ballif, Fulton and Liddell [2] drew attention to three important physiological criteria of the acute spinal condition: (i) Great depression of stretch reflex with disappearance of decerebrate rigidity; (ii) increased inhibitability of the knee-jerk; and (iii) prolongation of the jerk due, as is now known, to predominant participation of "slow" "red" muscle fibres after transection of the cord. Since the vestibulospinal tract is the chief descending pathway in the region of cord found essential for decerebrate rigidity, we have undertaken to destroy the tract at its origin by making lesions in the vestibular area of the medulla, and we propose to describe the results in the present paper.

METHOD.

Destruction of the vestibular nuclei.—Certain previous writers Gray [7]; Papez [11]; Allen [1], &c., have employed the method of inserting a probe perpendicularly through the cerebellum into the brain-stem, at a point corresponding to Deiters' nucleus. Although this operation has the advantage of being relatively simple surgically, it is undesirable since accuracy is difficult, and destruction of cerebellar tissue is entailed as well as the likelihood of injury to deeper structures in the medulla, e.g., rubrospinal tract. In an investigation on the cerebellum [6], we found that a satisfactory approach to the floor of the fourth ventricle could be secured under "dial" anæsthesia [5] by exposing the caudal half of the cerebellum and gently elevating the posterior vermis. With the medulla thus uncovered we found that by means of a small, slightly-curved red-hot needle about 1 mm. in diameter, it was possible to make a satisfactory lesion in any part of either vestibular region. Injury to the cerebellar peduncles as well as to the posterior longitudinal bundle and the gracilis and cuneate nuclei can be avoided by this technique. The details of our surgical approach are fully described in our forthcoming paper on the cerebellum [6].

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[1] A preliminary note under the same title has appeared in the *Journal of Physiology* (1930, **70**, *Proc.*, xxii).

Recording.—In acute experiments, vestibular lesions have generally been made under profound anæsthesia immediately after decerebration; but in some experiments the lesions were made some hours after the animal was decerebrated. The usual dissections were then made previous to myographic examination, i.e., isolation of both quadriceps muscles and complete denervation and immobilization of all other muscles in both hind limbs. Photographic records of responses were obtained with the new frictionless torsion-wire myograph [4], simultaneous electrical records being made with an Einthoven string galvanometer in the same optical system. For inhibition maximal single break-shock stimuli from a coreless Berne inductorium at 3 cm. applied to the ipsilateral popliteal nerve were used in all experiments. The stimuli were applied by means of Sherrington glass-shielded electrodes.

In our "chronic" animals, daily clinical observations were made before the myographic examination, which took place at the end of three weeks. After myographic examination, the spinal degenerations were studied by Marchi's method with no essential modification, except for prolonged washing after the tissue had been removed from dichromate. As yet only the spinal degenerations have been studied in detail and the medulla and cerebellum have been preserved to await detailed anatomical analysis. Since such factors as local œdema, &c., cannot be controlled in fixed preparations, the extent of acute lesions has only been studied macroscopically in fixed material. In one instance, however, we cut serial sections 20 μ thick through the region of the lesion after formalin fixation, staining every tenth section with hæmatoxylin and eosin.

I.—ACUTE EXPERIMENTS.

If, when decerebrate rigidity has appeared after mid-collicular transection of the brain-stem, a small lesion is made by inserting the red-hot needle into the medulla oblongata at a point 2-3 mm. from the midline at the level of the lateral angle of the fourth ventricle, the rigidity on the side of the lesion becomes much less within 1-2 minutes. If the lesion is made within 1 mm. of the midline little or no change is likely to occur. When the lateral area has been destroyed in this way, the resulting asymmetery may be so marked that if the preparation is supine the two limbs opposite to the lesion may be rigidly extended, while those on the same side lie in a flaccid, flexor posture on the surface of the body. To inspection the knee-jerk on the injured side is pendular in character, as in human cases with hypotonia. When examined myographically the quadriceps muscle shows a diminished or completely absent stretch reflex on the injured side, and the jerks tend to be more prolonged in duration as a result of the predominant participation of the red-fibred constituents of the muscle. Occasionally, following a vestibular lesion, we have observed " mixed " jerks in which a distinct white-fibred component is seen followed by a delayed relaxation characteristic of the red-fibred component and quite distinct from the "hump" of decerebrate rigidity, the latter being accompanied by action currents while the red-fibred "delay" shows no corresponding disturbance in the electrical record. Another significant distinction is that on the injured side the knee-jerk is more readily inhibited by single break-shocks, but the susceptibility to inhibition is less marked than in a spinal preparation. For comparison the curve of recovery of the jerk following a single inhibitory shock can be readily obtained on the two sides, as in the following figure taken from the experiment described below. It will be seen that on the intact side a single inhibitory shock is effective for less than 600σ, while on the injured side it is effective for $1{,}000\sigma$.

All our experiments have given essentially the same results, and the ensuing protocol will serve to illustrate the character of the observations.

June 17, 1930.—A young cat, weight 2 kg., was prepared under profound ether-chloroform anæsthesia, the two hind limbs being completely denervated except for the two quadriceps muscles.

Lesion in the right Deiters' area.—The cerebellar region was exposed by separation of the neck muscles, and the floor of the fourth ventricle brought into view by elevation of the posterior vermis. The preparation was then decerebrated at the mid-collicular level and after decerebrate rigidity had come on a curved red-hot needle was carefully inserted into the medulla at a point 1·5 mm. to the right of the midline, and was carried outward about 2 mm. from this point toward the apex of the lateral angle of the fourth ventricle. Respiration stopped momentarily, but was resumed again without recourse to artificial respiration.

Clinical observations.—Within three to four minutes after the lesion there was an evident diminution in the rigidity on the right side and the difference between the two sides became more and more marked in the course of the next hour. Three hours after the lesion had been made the left fore-limb was rigidly extended, and the right fore-limb lay flaccidly on the table. The difference persisted in all positions of the animal. The general condition of the preparation in respect to heart and respiration was entirely satisfactory and the pinna and conjunctival reflexes were active. The left knee-jerk to inspection was quicker than the right, and the right showed the pendular fling characteristic of hypotonia.

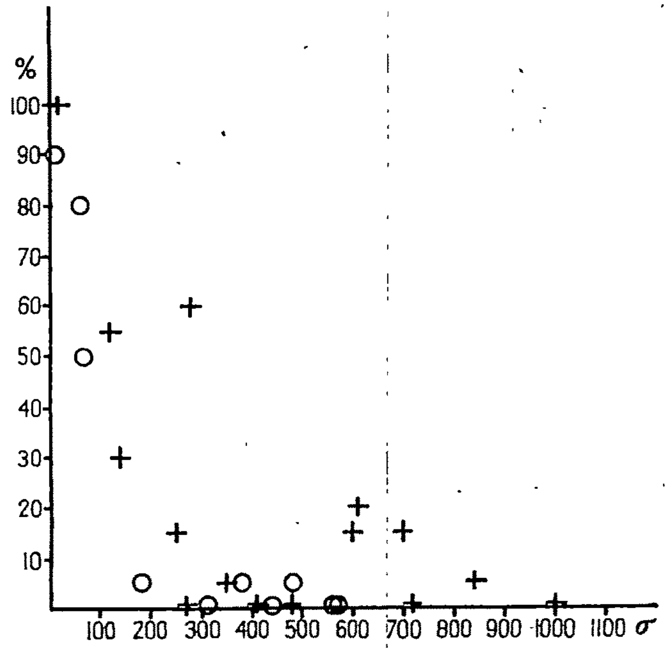

FIG. 1.—Acute experiment, described in text. Injury of medulla oblongata on right side. Ordinates = degree of inhibitory depression of response expressed as percentage of a normal response to a series of equal taps. Abscissæ = time in sigmata after inhibition. + Right vasto-crureus. O Left vasto-crureus.

Myographic examination.—When attached to the myograph the stretch reflex of the right quadriceps, though present at first, was not sustained and soon vanished completely. The knee-jerk was large, slow and required a high initial tension for its elicitation. There was no trace of a white-fibred component. The jerk was readily inhibited and the curve of recovery following a single break shock inhibition is shown in fig. 1. The crossed extensor reflex was difficult to elicit and of brief duration, exhibiting but little after-discharge.

The left quadriceps on the other hand showed quick brisk knee-jerks, a marked and well-sustained stretch reflex and the jerks were considerably more difficult to inhibit than on the right side, but it appeared that they were more susceptible than the jerks of a normal decerebrate preparation. Crossed extensor reflexes were brisk and well-sustained.

Neck and labyrinthine reflexes.—Despite the fact that the neck muscles had been freely resected, turning of the head caused evident effect in the *left* quadriceps, there being a spontaneous increase in rigidity on turning it maximally and diminution when in the minimal position. With the *right* quadriceps the neck reflexes were only just present and were scarcely perceptible, maximal turning being required to produce 50—100 grm. spontaneous increase in tension.

Pathological note.—The medulla oblongata and upper spinal cord were fixed in formalin and embedded in paraffin. Serial sections 20μ thick were cut and every tenth section mounted and stained with eosin-hæmatoxylin. The lesion involved the right dorso-lateral surface of the medulla, extending from the rostral poles of the nuclei of Goll and Burdach forward into the middle peduncle of the cerebellum. The whole of the descending vestibular nucleus and the caudal third of Deiter's nucleus were completely destroyed. More rostrally the dorsal portion of Deiter's nucleus, the nucleus of Bechterew and the lateral portion of the medial vestibular nucleus were destroyed. The lesion cut the restiform body and in the middle cerebellar peduncle extended dorsally to the ventral portion of the nucleus emboliformis. Only the most rostral fibres of the uncinate fasciculus of Russell escaped.

II.—CHRONIC EXPERIMENTS.

With aseptic precautions the region of the right vestibular nuclei was cauterized in four cats as described above. The protocols of two of the experiments are given in detail below. All four of the animals showed the usual clinical picture, of which the most prominent features were as follows: nystagmus, forced rolling movements to the side of the lesion, asymmetrical postures, and hypotonia of both homolateral limbs. In all cases the intensity of the symptoms became considerably less marked with time.

Animal II.

Operation, May 2, 1930.—Under "dial" anæsthesia the usual cerebellar exposure was made, and the posterior lobe of the vermis was elevated. The red-hot needle was then thrust gently into medulla at a point 2 mm. to the right of the midline slightly caudal to the lateral angle of the fourth ventricle. The needle was inserted a second time to destroy some of the superficial area around the first lesion. There was no bleeding and the wound was closed as usual in layers.

Post-operative course.—The animal began to come out of the anæsthetic within twenty-four hours and took fluid and solid food after two days. Its general condition and nutrition remained excellent. There was slight weakness of the right side of the face for three or four days, with complete recovery from this within a week.

Forced rolling movements developed as the anæsthetic wore off and were most marked for the first four days after operation. During this period, when placed on the floor, the cat would roll to the right until its progress was impeded by some obstruction. From the fifth day the rolling movements became gradually less, and had practically stopped by the thirteenth day. The *posture* was asymmetrical throughout the period of observation, the head being turned with the occiput to the right, the chin to the left. For the first few days the cat braced itself against the back of the cage, but later it lay curled up with the head and tail bent to the left, although the head remained rotated as described above. A rapid rotatory *nystagmus* appeared as the anæsthetic wore off, the quick component being clockwise, the slow component anticlockwise. This was very marked and almost continuous for the first four days, but then gradually diminished and disappeared between the eighth and twelfth days. There was marked *hypotonia* of the right fore and hind-limbs on the first day after operation, which continued throughout the period of observation, although it was less marked at the end of two weeks. The *knee-jerks* showed a similar difference, the left being noticeably brisker and the right being pendular. A slow shaking *tremor* of the head and shoulders appeared as the rolling movements decreased and remained present throughout the period of observation, although it was never a very marked symptom.

On the last day of observation, the twenty-first day after operation, the animal was able to walk in a crouching position, the trunk and tail held stiffly, the head rotated slightly (chin to the left). It was very unsteady, frequently falling to the right. There was a definite limp on the right hind leg. When held up by the scruff of the neck this leg hung lower than the left, although the tone of the fore-limbs was approximately equal. The right knee-jerk was pendular, and the scratch reflex on the right showed a longer latent period than that on the left. There were only occasional nystagmoid jerks on lateral deviation.

Myographic examination. May 23.—Under deep chloroform-ether anæsthesia the preliminary dissection of the hind limbs was made after which the cat was decerebrated by intercollicular section through a trephine opening in the skull. Good extensor rigidity developed within ten minutes of decerebration and was definitely more marked on the left than on the right. The general condition of the preparation with regard to heart and respiration remained good throughout the period of observation.

Three hours after decerebation the preparation was arranged for myographic recording. Observations were made first from the right and then from the left quadriceps. At the end of the experiment it was again noted that on holding the preparation symmetrical and supine the left fore-limb showed good extensor rigidity, while the right fore-limb sunk down partially flexed.

A *stretch reflex* was present on both sides, but definitely more pronounced left than right. Inhibition of the stretch reflex on stimulation of the ipsilateral peroneal nerve was less complete on the left.

The *knee-jerk* on the right was of long duration, and there was rather marked inhibition following stimulation of the ispilateral nerve. On the left the jerks were of shorter duration and were somewhat irregular, but the inhibition was less pronounced. A comparison of the rate of recovery from inhibition may be made by reference to fig. 2.

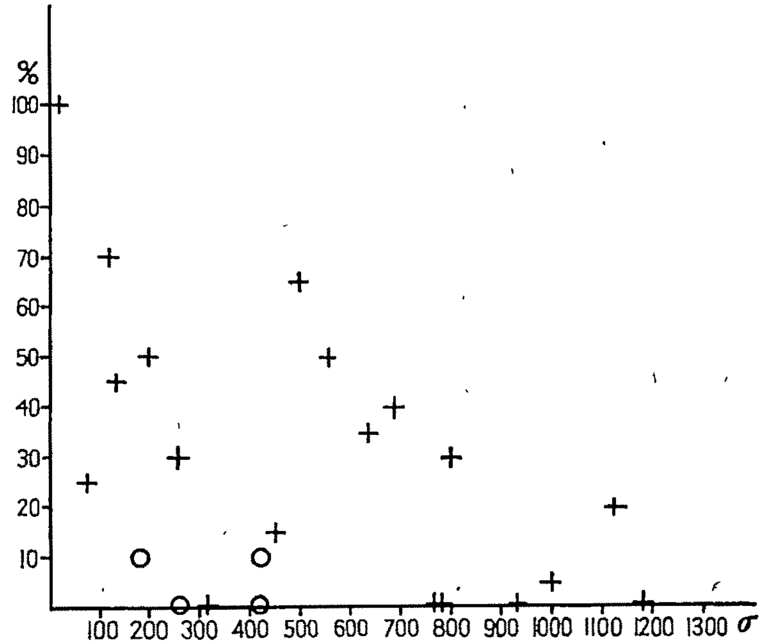

FIG. 2.—Chronic experiment, Animal II, described in text. Injury of medulla oblongata on right side. Ordinates and abscissæ as in fig. 1. + Right vasto-crureus. O Left vasto-crureus.

The *crossed extensor reflex* was observed on both sides, the response of left muscle being smaller than that of the right. With the head in the intermediate position the response was small and quick, but with the head rotated either toward or away from the muscle, the response was large and longer.

The *labyrinthine and neck reflexes* were repeatedly observed in both muscles and it was constantly found that with the head turned to the maximal position the resting tension in the muscles was higher, and there was less inhibition of the jerk, but with the head in the minimal position, the resting tension of the muscles was lower and the jerk somewhat more readily inhibited.

Pathological note.—Macroscopical examination of the medulla showed a scar in the right dorso-lateral region which involved the vestibular nuclei, the restiform body, and the middle portion of the middle peduncle of the cerebellum. The brachium conjunctivum was intact. Sections from the cervical, thoracic and lumbar cord, stained by the Marchi method, showed heavy degeneration in the direct vestibulospinal tract on the right side (fig. 3.) There were less heavy degenerations in the marginal fasciculus, in the region of the medial reticulo-spinal tract of Papez [11], and of the descending vestibular component to the medial longitudinal fasciculus of the homolateral side described by Rasmussen [13]. In the cervical section there were also scattered degenerations in the region of the crossed vestibulospinal tracts of Gray [7], and the region of the homolateral rubrospinal tracts, but these were no longer seen in the sections from the thoracic cord.

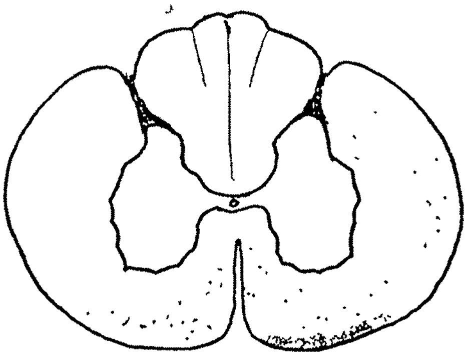

FIG. 3.—Degenerations in Animal II from the cervical level.

Animal V.

Operation. May 14, 1930.—A cerebellar exposure was made under "dial" anæsthesia and the posterior lobe of the vermis elevated. The right vestibular area was then cauterized by twice inserting the red-hot needle about 2 mm. from the midline, approximately at the level of origin of the eighth cranial nerve. There was no change in respiration and no bleeding. The incision was closed in the usual manner with discontinuous silk sutures.

Post-operative course.—The animal began to come out of the anæsthetic in thirty-six hours, and took food and fluid on the second day. Its general condition remained excellent throughout the period of observation. *Forced rolling movements* appeared as the anæsthetic wore off, and were very marked from the third to the fifth day after operation, the animal rolling to the right across the floor until it was stopped by some obstacle. Compensation occurred rapidly, and by the eighth day the animal was able to sit in a horizontal position, although there was some swaying, and it was apparently dizzy. The *posture* during the period of observation was asymmetrical, the head being rotated, and also bent to the right, but there was no tremor.

For the first six days post-operative there was a spontaneous lateral *nystagmus*, the quick component to the left, the slow component to the right. This symptom then subsided. *Hypotonia* was present throughout the post-operative period in both limbs of the right side, being more marked in the hind-limb than in the fore-limb. Comparing the two hind-limbs, the *knee-jerks* remained equally brisk, but on the right they were pendular, whereas on the left they were normal. The *righting reflexes* were normal after the first ten days. If the cat was placed on its back it came to the horizontal position by turning either to the right or to the left, whichever direction was shorter.

On the last day of observation—the twenty-third day after operation—the animal was able to run in a half-crouching position, the body at an angle of 15-20° with the direction of the line of motion. It was unsteady and frequently fell, usually to the right, but occasionally to the left. There was definite limp of the right hind leg, and several times this leg collapsed under the weight of the body. When held up by the scruff of the neck there was a slight tendency to bend towards the right. The knee-jerks were active and essentially equal, there was no positive supporting reaction, and the scratch reflex was slightly more active on the left than on the right.

Myographic examination. June 6, 1930.—Under deep chloroform-ether anæsthesia the preliminary dissection of the hind-limbs was carried out, after which the cat was decerebrated. Good decerebrate rigidity developed in fifteen minutes, and was much more marked on the left side than on the right. Three hours later the preparation was attached to the myograph for recording first from the right and then from the left quadriceps in the same manner as in previous experiments. The general condition of the preparation remained good throughout the period of observation, and the difference in rigidity of the two fore-limbs was unaltered.

There was a slight *stretch reflex* present in the left quadriceps which was only very slightly inhibited by stimulation of the ipsilateral peroneal nerve. On the right the stretch reflex was slightly larger, but it was markedly inhibited by the same strength of stimulus. The *knee-jerks* were very similar on the two sides, being small and fast (average duration 60σ), but the knee-jerk on the left was more easily inhibited than in a normal decerebrate preparation, and on the right the inhibition was still more marked. *Labyrinthine* and tonic *neck reflexes* were present on both sides, but were more pronounced on the right than on the left. In each case the resting tension of the muscle was increased by turning the head to the maximal position and decreased by turning the head to the minimal position. The susceptibility to inhibition of the knee-jerk was less when the head was maximal and greater when the head was minimal. The crossed extensor response was also observed to be greater with the head maximal than minimal.

The *crossed extensor reflex* was at first elicited by applying alternating make and break shocks to the contralateral peroneal nerve by moving the camera key with the finger. It was noted that on the left there was a good response which summed readily and relaxed slowly, but on the right the excursion was not so ample though the character of the response was much the same. Later the crossed extensor response was elicited by applying a tetanizing current from a neon tube oscillator to the contralateral nerve. On the right there was a large well-maintained response which recovered from partial inhibition from a single shock to the ipsilateral peroneal nerve, but on the left the response was very poorly maintained and there was no recovery after inhibition.

Pathological note.—Macroscopical examination of the medulla showed a slight scar of the caudo-lateral surface of the floor of the fourth ventricle, which continued rostralward into the middle cerebellar peduncle. The scar involved the major portion of the vestibular nuclei, especially the lateral nucleus. The restiform body and the brachium conjunctivum were intact. The degenerations in all parts of the cord were similar to those described in Animal II (see fig. 4), with the exception that there was practically no degeneration in the region of the homolateral rubrospinal tract.

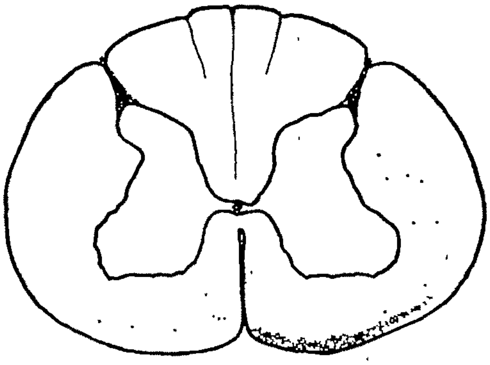

FIG. 4.—Degenerations in Animal V from the cervical level.

CHRONIC EXPERIMENTS. SECTION OF EIGHTH NERVE.

In three cats the left eighth cranial nerve was divided through a cerebellar approach. The protocols of two of these experiments are given in detail below. All of the animals showed symptoms of forced rolling movements to the side of lesion, asymmetrical posture and nystagmus. A fourth symptom deserves mention: for several days after operation the tonus of the limbs was almost equal on the two sides, there being a slight hypotonia of the homolateral limb, but later this changed to a definite *hypertonia* of the homolateral limb which amounted almost to an extensor rigidity in the case of the second animal. In this respect the clinical picture following section of the eighth nerve is exactly opposite to that seen following the destruction of the vestibular nuclei, though in other respects the symptoms from these two lesions are much the same

Animal I.

Operation. April 29, 1930.—Under "dial" anæsthesia a cerebellar exposure was made and the opening through the occipital bone enlarged to the left with rongeurs. The dura was then freely resected, and a narrow retractor introduced into the left cerebello-pontine angle to retract the lateral lobe of the cerebellum upwards and forwards and the medulla slightly medialwards. By this means a view could be obtained of the eighth nerve just as it emerged from its bony canal. The operation was complicated by slight oozing of blood, but after two attempts the nerve was sectioned with ophthalmological scissors. When hæmostasis was complete the wound was closed in layers.

Post-operative course.—The animal remained deeply narcotized for thirty-six hours, and did not take food or fluid until the fourth day. After that it fed and drank normally and its general condition remained satisfactory. There was a partial paralysis of the left side of the face, apparently due to accidental injury to the seventh cranial nerve at operation. *Forced rolling movements* to the left developed as the anæsthetic wore off, and were very marked for five days, following which they rapidly subsided and disappeared entirely on the ninth day. During the first part of this period attacks of rolling could be induced by a loud noise if the cat was lying quietly, or by sensory stimulation such as rubbing the back. The *posture* was asymmetrical throughout the period of observation, the head being bent to the left, and the chin slightly rotated to the left. This asymmetry was more marked during the first week after operation than later. When picked up by the scruff of the neck the head was bent to the left, the tail to the right, the left fore-limb was extended forward, the right semi-flexed, the left hind-limb was extended backwards, and the right drawn forwards. A slow oscillating *tremor* of the head and shoulders was noted on the eighth day after operation when the animal first attempted to walk. This tremor remained constant during any voluntary activity throughout the remainder of the period of observation. At the end of two weeks the animal was able to crawl along the floor, and at the end of three weeks was able to walk in a crouching position, turning to the left and frequently falling to the left, although it occasionally also fell to the right. There was definitely poor balance, but there was no weakness of the limbs on the side of the lesion, as was noted in the cat with destruction of the vestibular nuclei.

During the first week after operation there were frequent rapid jerks of the eyes to the left with a slow return to the right, although there was no sustained *nystagmus.* After the first week the eye movements were normal. There was slight *hypotonia* of the left fore- and hind-limbs for two or three days following operation, but this decreased and the tone of the limbs became equal. Later the limbs on the left showed a definite hypertonia amounting to spasticity of the left fore-limb at the end of three weeks. The knee-jerks were equal throughout the period of observation. On the last day of observation—the twenty-seventh day after operation—the cat was able to walk, though with considerable difficulty. It crouched close to the floor, frequently falling, more often to the left than to the right. The legs were moved with some uncertainty, and there was considerable oscillating tremor of the head and shoulders. When held up by the scruff of the neck, the head was bent to the left and the chin slightly rotated towards the left also. The left fore-leg was stiffly extended close to the body, the claws also being extended, the paw slightly flexed. The right fore-limb was semi-flexed. Both hind-limbs hung moderately loose, but the left was slightly more extended than the right, and showed slightly more tone. The toes of the left hind paw were held continuously extended, but were flexed on scratching the pad. On the right the toes were flexed. Knee-jerks and scratch reflex were active and equal. There was no nystagmus.

Myographic examination. May 26, 1930.—Under deep chloroform-ether anæsthesia the preliminary dissection of the hind-limbs was made, after which the cat was decerebrated by intercollicular section. Three hours later the preparation was attached to the myograph in the usual manner, and records were taken from the right and from the left quadriceps femoris. It was noted that when the cat was held symmetrically in the supine position that the resting tension of the fore-limbs was greater on the left than on the right.

There was a good *stretch reflex* on both sides, but it was greater on the right, and on the right there was marked inhibition of the stretch reflex by a single break-shock to the ipsilateral peroneal nerve, whereas on the left there was only slight inhibition. The *knee-jerks* were very fast on both sides, the average duration being 40σ. There was only slight inhibition of the jerk, more marked on the right than on the left.

Neck and labyrinthine reflexes were very marked on the right side, the resting tension of the muscles being much higher with the head in the maximal than in the minimal position. Turning the head had no detectable influence either on the left stretch reflex or upon the inhibition of the jerk.

The *crossed extensor response* on the right, with the head in the maximal position was large, showing a rapid rise with a slow descent and excellent summation. With the head in the neutral position the crossed extensor response was small, and with the head in the minimal position there was no response. On the left with the head maximal, the crossed extensor response was small and subsided slowly. With the head minimal the response was definitely smaller and subsided faster.

Pathological note.—At necropsy the eighth nerve was found to be completely transected. Macroscopical examination of the medulla after fixation in 5 per cent. formalin showed some hæmorrhagic discoloration of the tissue around the point of entrance of the eighth nerve. This discoloration extended 2 or 3 mm. rostralward into the middle cerebellar peduncle.

Animal IV.

Operation. May 8, 1930.—Under "dial" anæsthesia the left eighth cranial nerve was transected in the manner already described.

Post-operative course.—The animal was old and made a very slow recovery from the operation. It was not completely out of the anæsthetic until the fourth day, and did not take food or fluid until the seventh day, after which it fed normally. The further post-operative course was complicated by a complete left facial paralysis. *Forced rolling movements* developed as the anæsthetic wore off and were very severe for the first eight days, the animal rolling rapidly to the left until it met some obstruction against which it could brace itself. When lying still in the cage these attacks of rolling might be brought on by a loud noise or by stimulation of the skin. During the second week the animal would lie partially on its right side with its legs braced out to the left to prevent its rolling. The rolling movements gradually stopped between the twelfth and fourteenth day. Throughout the period of observation the *posture* was asymmetrical, the head being bent to the left and the chin rotated slightly to the right.

There was a marked spontaneous lateral *nystagmus*, the quick component to the right after operation. This became less during the second week and disappeared during the third week. During the first week after operation there was moderate hypotonia of the left fore- and hind-limbs, but during the second week this changed to a hypertonia of all four limbs, and much more marked on the left side. The *knee-jerks* were at first equally brisk with some fling to the left leg. During the third week, however, the left knee-jerk was more brisk than the right. In the first week the scratch reflex was active on the right but absent on the left. Later, however, the scratch reflex was equal and active on the two sides.

On the last day of observation—the twenty-fifth day after operation—the animal lay quietly in its cage in the horizontal plane with the head and body flexed to the left and the chin rotated slightly to the left. It was able to crawl forward a few steps on the floor in a crouching position, turning and falling to the left. The righting reflexes were active, and were apparently equal on the two sides. When held up by the scruff of the neck the head and tail were flexed to the left, the left fore-limb was stiffly extended closely to the body, the ankle slightly flexed, the claws extended ; the left hind-limb was stiffly extended backwards, the toes spread. On scratching the pads of the left foot, however, the toes were flexed. The right fore- and hind-limb were partially flexed. The left knee-jerk was brisker than the right; and the scratch reflex showed a longer latent period on the left than the right.

Myographic examination. June 2, 1930.—Under deep chloroform-ether anæsthesia the same dissection of the hind-limbs was performed as described in the experiments above, and the cat was then decerebrated by intercollicular section through a trephine opening in the skull. Good decerebrate rigidity came on in fifteen to twenty minutes, and was much more marked on the left than on the right side. The left knee-jerk was much more active than the right to inspection. Three hours later the preparation was attached to the myograph. The general condition of the preparation remained good throughout the period of observation. Records were iaken from the right and left quadriceps.

Stretch reflex was pronounced on the right, and was markedly inhibited by a single break-shock to the ipsilateral peroneal nerve. On the left the stretch reflex was not so marked, and there was only very slight, if any, inhibition. The jerks on both sides were small and very fast, averaging 40σ in duration, and there was no inhibition of any of the jerks.

Neck and labyrinthine reflexes were active on the right, the resting tension of the muscle being much higher with the head in the maximal than with the head in the minimal position. On the left, however, there was scarcely any change of the stretch background by changing the position of the head.

The *crossed extensor* response on the right was slight with the head in the maximal position, but absent with the head in the minimal position. On the left side the results were the same, but with even less pronounced differences.

Pathological note.—At necropsy the eighth and seventh nerves of the left side were found to be completely transected, and there were some adhesions to the caudal margin of the left lateral cerebellar lobe, and to the adjoining region of the medulla

DISCUSSION.

In a previous paper [4] it was shown that the knee-jerk became changed from the decerebrate form to the spinal form when lesions of the homolateral anterior column of the spinal cord were made. The chief descending fibre tracts in this region of à cat's cord are as follows: the tectospinal fasciculus, consisting of both crossed and uncrossed fibres; the reticulospinal fasciculi described by Papez [11], and the vestibulospinal fasciculæ.

It is unlikely that the tecto-spinal system exerts any great influence in the present problem since within quite wide margins the level of decerebration has little effect on the form of the knee-jerk or its susceptibility to inhibition. No definite conclusions, however, can be drawn from the present series of experiments regarding the influence on the knee-jerks of the reticulospinal tracts of Papez. That they play a rôle in the susceptibility to inhibition is probable from the fact that complete section of the homolateral anterior column of the spinal cord has a greater effect on the knee-jerk than a large lesion in the vestibular nuclei in the medulla.

The origin and course of the vestibulospinal tracts have recently been described and discussed by Gray [7] who found a direct and a crossed vestibulospinal tract. The former originates in the lateral nucleus of Deiters and passes caudally in the ventro-lateral column through the entire length of the cord. The latter originates in the descending vestibular nucleus of Schwalbe as the lower arcuate fibres, to cross the midline and descend in the medial longitudinal fasciculus of the opposite side through the entire length of the cord. Both tracts terminate in the ventral gray column. Rasmussen [13] confirmed these observations, and also found that a number of fibres from the descending vestibular nucleus passed caudally down the cord in the homolateral medial longitudinal fasciculus. As we have shown that only lesions which reach the midline affect the knee-jerk and that lesions of the vestibular nuclei increase the inhibition of the knee-jerk of the contralateral side it is evident that both crossed vestibulo-spinal tracts (which run in the marginal fasciculus) as well as the direct (in the ventrolateral fasciculus) play a rôle in the control of spinal motor centres. It is also evident from the present experiments that the direct tract is the more important of the two.

In investigating the medullary centres influencing the tonus of skeletal muscle, Spiegel [15] found that lesions affecting Deiters', the medial vestibular and the descending vestibular nuclei cause considerable diminution of the rigidity in decerebrate preparations. He also found with lesions which extended more medially and involved the reticular substance of the medulla and the vestibular nuclei that there was complete loss of " tonus " on the homolateral side. All of his experiments, however, were acute, the medullary lesions being made through the posterior approach shortly after rigidity had appeared following decerebration. He concluded that the vestibular nuclei were not solely responsible for the rigidity seen in decerebrate preparations. Further evidence was supplied by the fact that in certain operations the vestibular nuclei of one side were destroyed with diminution of rigidity on the same side, following which the vestibular nuclei of the opposite side were destroyed with return of complete decerebrate rigidity instead of bilateral diminution which might be expected.

Our observations harmonize in general with those of Spiegel, and they also indicate that the lateral vestibular nucleus of Deiters and its descending spinal pathway is undoubtedly the most important of the medullary centres essential for the maintenance of decerebrate rigidity. The results suggest that this nucleus exerts its influence by diminishing the susceptibility to inhibition of the extensor centres in the spinal cord, and we would urge once more [4] that the condition of spinal shock which results when the vestibulospinal pathway is severed is due chiefly to the greatly increased susceptibility to inhibition of the lower spinal centres.

The correlation between the flaccidity observed clinically after a vestibular lesion and the absence of stretch reflex observed myographically is worthy of note, and it bears further evidence of the basic character of the stretch reflex in the maintenance of posture [8], [9].

Section of the eighth nerve causes an augmentation of posture on the same side and the effect is in every respect the opposite of a lesion of the vestibular nucleus. The rigidity and stretch reflexes are increased on the same side and the knee-jerk is more difficult to inhibit.

Summary of Conclusions.

(1) Experimental lessons of the vestibular nuclei in normal animals cause hypotonia on the side of the lesions, forced rolling movements to that side. If decerebrated after an interval of three weeks, the rigidity and stretch reflexes are greatly diminished on the injured side, and the knee-jerk is more readily inhibited. Marchi staining of the cord in such animals has shown extensive degeneration of the homolateral vestibulospinal pathway and slight degeneration in the crossed vestibulospinal tract.

(2) Acute lesions of Deiters' area *after* decerebration also cause great diminution of rigidity on the same side and increased susceptibility of the knee-jerk to inhibition.

(3) We conclude that the nucleus of Deiters and the direct spinal pathway to which it gives rise is chiefly responsible for the differences between the decerebrate and the spinal condition, and hence its integrity is essential for preventing spinal shock.

Addendum.—After our paper had gone to press, we learned that our friend Dr. Paul Martin, of Brussels, had carried out similar experiments and had reached the same conclusions on the modification of the knee-jerk after acute vestibular lesions. Dr. Martin began his experiments six months before ours were undertaken.

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THE ELECTROMYOGRAM OF VOLUNTARY MOVEMENTS IN MAN.

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I.—Electromyograms of Voluntary Movements in which Electrical Effects contributed to by a whole Muscle are recorded with a String-Galvanometer.

Voluntary contraction of a muscle is associated with changes in electrical potential of the tissues immediately surrounding it. These changes have been recorded as deflections of a galvanometer connected to a pair of electrodes placed upon the skin overlying the muscle. In the numerous investigations of these electrical changes or "action currents" as they have been called, it has been the custom to place the electrodes in a line with the long axis of the muscle, and either strapped upon the surface of the skin or penetrating this to make direct electrical contact with the subcutaneous tissues beneath.

The deflections or oscillations will be completely determined if we know their form, their amplitude and their frequency. It is therefore in terms of these three characteristics that they will be described and their variations under differing conditions discussed.

The form of the oscillations.—In the course of his measurements of the latent period of skeletal muscle, Hermann [35] noticed that the electrical changes did not appear simultaneously in all parts of a composite muscle. From a study of their temporal distribution he put forward the idea of a " nervous centre of gravity " of each muscle and described the transverse plane in which this lies as the nervous "equator." His conception, that waves of activity originate in the nervous equator and spread from it up and down the length of the muscle, has been accepted by most subsequent workers, who have agreed with Hoffmann [38] that the electrodes should be placed close together and towards one end of the muscle in order to get deflections of the greatest regularity and amplitude.

Using these conditions, nearly all investigators have found that the oscillating record obtained consists of a series of diphasic deflections, although a few have stated that polyphasic variations in potential are usual (Judin [43]) or constant from certain muscles such as the tibialis anticus (Wacholder [71]). In addition to these comparatively short-lasting oscillating changes in potential, long drawn-out, monophasic shifts of the base line of the record have been described. Most of such effects were originally due to polarization at the surface of the electrodes, but they may also occur when this is avoided and are then due to mechanical shifting of the position of the electrodes on or in the tissues (Gregor and Schilder [31]). Adrian [1] has pointed out that polarization can have no effect upon the form of the quick, phasic oscillations and holds that such mechanical shifting of the electrodes accounts for the maintained alteration in potential which Lewy [48] found to be normally associated with muscular activity.

The amplitude of the oscillations.—Voluntary movements in man give, under the above conditions of recording, electromyograms which do not show deflections of regular amplitude. They stand thus in contrast with reflex movements in man and other vertebrates, and with the normal movements of arthropods (Hoffmann [38], p. 727), Ewald [20]).

In any one record the oscillations usually vary continuously from those of just visible size up to those of maximal size determined by the nature of the electrodes and the sensitivity of the recording apparatus. Although this variation in size is continuous, most observers have described the deflections as falling into two groups: large, primary or " A " waves of lower frequency, and small, secondary or " B " wavelets of higher frequency. Others have carried this differentiation a step further and have separated three different types, primary and secondary waves, and "Nebenzacken" (Richter [59]). The original view was that the two chief types of deflection were attributable to two different sources or to two different series of phenomena associated with the muscular contraction, and by some this view is still held. Thus Wacholder [72], although agreeing that the graduation is continuous, believes that the difference between the two types, large and small, which may be simultaneously recorded leaves no room for doubt that they are of different origin.

v. Weizsacker [76], in his study of electromyographic changes in certain pathological states, observed that the same degree of contraction of the muscle may be associated with differing records, but that comparison of these records shows that the average amplitude of the oscillations is roughly inversely proportional to their frequency. From this he infers that the total number of electrical impulses coming from the muscle may be constant for any given degree of contraction, and that these impulses will give many small oscillations or a few large ones according to their degree of overlap or fusion. In support of this inference he points out that if during the maintenance of a voluntary effort, which is giving an electromyogram of the normal irregular type, a series of tendon-jerks are elicited in the muscle used, the electromyogram now shows a corresponding series of especially big deflections with silent intervals between.

This view of the deflections as being contributed to by many different parts of the muscle each of which produces electrical changes in its surroundings as it becomes active, and as having varying amplitudes determined by the degree of fusion of the effects of these constituent parts, is now generally accepted. It is clear that this fusion will depend upon the relations of the individual muscle-fibre groups to the electrodes and upon their relative synchronization. When these groups of fibres which are contributing the electrical changes are mainly synchronized and a few only are out of phase, the tendency will be for the records to contain a few large deflections corresponding to the majority in-step, together with many small deflections corresponding to those out of phase or unsynchronized. Many observers have noted the disappearance of the smaller oscillations when regular, larger ones appeared, and Wacholder [70] refers explicitly to the association between the sudden, simultaneous increase of amplitude and of greater synchronization of the innervation impulses to the muscle recorded.

If this view, that differences in amplitude of the deflections are due to different degrees of synchronization of the muscle-fibres, be correct then the amplitude cannot be expected to give any measure of the force of the contraction. This conclusion is supported by Adrian [1] and Wacholder [74] in their reviews of this subject.

A discussion of the variations in amplitude which have been described can, for these reasons, be more usefully postponed until the question of innervation frequency is considered.

The frequency of the oscillations.—Comparison of the figures given by different observers for the deflection frequency is complicated by three factors :—

(1) Some observers have counted the waves of different size-groups separately—others the total number of waves irrespective of size.

(2) Differences in galvanometer sensitivity lead to great differences in the appearance of the records obtained. Where total deflections are in question, this leads to an apparent reduction only in frequency of the less sensitive records, due to the fact that some of the deflections are too small to be noticed. Where different size-groups are counted separately, it leads to a relative diminution of the frequency of the group of larger deflections when the sensitivity is decreased.

(3) In connection with few records have the conditions of recording been adequately described—in particular in respect of the tension developed by the muscle at the time of recording.

In 1912 Piper [49] published his conclusion that the frequency of the large waves alone was 50 per second for all voluntary movements and was unaltered for different strengths of contraction. Subsequent workers have agreed that this rate is very often seen in the electromyograms of voluntary movements, more especially when the muscular effort is a large one, but that it may also be much lower. With increasing sensitivity of recording and with electrodes which are influenced by more strictly localized changes only, rates as low as 8-10 (Wacholder [74]) and 5-8 per second (Richter [59]) have been found associated with slight degrees of voluntary effort. Even when the greatest effort is made the rate has not been found to rise above 75 per second, and most observers give figures which suggest that the most common frequency for the large waves lies in the neighbourhood of Piper's figures. (Altenburger [3], 50-60; Bornstein and Sanger [11], 50; Gregor and Schilder [31], 37-70; Richter [59], 40-65; Wacholder [71], 50-75; Henriques and Lindhard [33], 40-65; Salamonson [61], 50; Proebster [53], 40; Cobb and Forbes [13], 40-58; Semereau and Weiler [64], 50.) The significance of this 50 per second rate has yet to be determined and will be discussed later.

The results of those investigators who have estimated the frequency of the smaller waves are still less comparable, because while with stronger voluntary effort the large waves tend to become more regular, the smaller waves become irregular and grouped, or disappear. With moderate degrees of contraction their rate has been variously estimated at from 50 to 300 per second. (Altenburger [3], 160-190; Wacholder [71], 150-180; Richter [59], 180-250; Proebster [53], 200; Pradwicz Neminski [57], 20-150; Trendelenburg and Schutz [68], 120.)

We are here considering the frequency of galvanometer-deflections, and in the light of more recent knowledge of the electrical field set up by active muscle and of the varying synchronism of innervation of different muscle-fibre groups, it is clear that no significance attaches to these figures. They could only have value if some assumption such as that made by Athanasiu [5] were correct, i.e., that the total muscle mass is always synchronously innervated. In this case also, the same author's suggestion that the ratio of the small to the large wave frequency tends to be constant (4 : 1) would be not so improbable. Since we have good grounds for supposing this suggestion to be invalid, such frequency measurements and their comparison are probably meaningless.

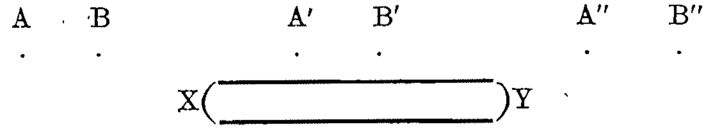
To summarize the evidence of the above paragraphs, we may state that the electromyogram of normal voluntary movements, as recorded by means of a string-galvanometer and surface electrodes, shows a series of diphasic deflections or oscillations. These are of irregular amplitude but fall roughly into two groups, large and small deflections, and they recur at the average rate of 50 per second and 180 per second respectively. With increasing muscle tension the galvanometer deflections show a rise in total frequency, an increase in average amplitude and no change in their individual form. These are only generalizations, and neither of the variables, frequency and amplitude, alter at any stage proportionately with the rise in tension. Moreover, a given tension in the same muscle repeatedly and similarly recorded, is not invariably associated with the same type of electromyogram. Thus it has been shown by Wacholder [70] that contraction and relaxation respectively, through a certain phase of muscle tension, yield quite different pictures, and that the same muscle used as an agonist, an antagonist, or as a synergist for different movements, gives a different record in each case.

The interpretation of these differences depends upon differences in the innervation and not in the forms of muscular activity, and the correctness with which we can infer the character of this innervation from the galvanometer deflections will be decided by our ability to determine the source of the potential differences recorded and the factors governing their appearance and form.

II.—The Electrical Field set up in the Surroundings of a Contracting Muscle.

A muscle strip isolated from all other structures and stimulated to contract shows a series of changes in electrical potential, "action currents," along its surface as the wave of mechanical activity spreads through it. In the light of the results previously obtained from the use of such isolated muscle preparations, it has proved difficult to interpret the galvanometric oscillations associated with the activity of intact muscles when electrodes are placed upon the surface of the body. Recently, however, the work of Craib has made this interpretation possible. He has shown [16] that the deflections resulting from activity of an isolated muscle preparation depend upon the amount and distribution of the conducting medium surrounding the muscle and upon the position of the electrodes within this medium in which is situated the electrical field. The records obtained from a muscle strip in air differ greatly from those given by the same strip when surrounded with saline solution, and Craib has studied the galvanometric responses obtained from electrodes placed in different parts of such a conducting medium. His observations have proved successful in the interpretation of the changes in electrical potential which accompany the activity of cardiac muscle, and we may look to them to provide a satisfactory interpretation of the electromyogram of voluntary contraction in skeletal muscle.

It is only comparatively recently that needle electrodes thrust right into the active muscle have been employed (Adrian and Bronk [2]). As has been pointed out, the electromyograms of voluntary movements previously published have been obtained by the use of electrodes placed either upon the surface of, or just beneath, the skin. It is with the interpretation of such electromyograms that we are now concerned, i.e., those recorded from what we may speak of as "distant" electrodes arranged parallel to the long axis of the muscle and towards one of its ends.



If in the above figure X—Y be taken to represent the active portion of the intact muscle and A—B, A′—B′, A″—B″, pairs of electrodes making contact with the surrounding tissues, we learn from Craib's work that as a wave of activity passes from X to Y a diphasic deflection will be recorded from A—B and A″—B″ and a polyphasic deflection from A′—B′. This last deflection will consist typically of six phases, three contributed by the passage of the active region beneath A′ and three by the passage beneath B′. These six phases are not of equal magnitude and they suffer various degrees of fusion which are dependent upon the length of the active region, the nearness of A′ to B′ and of A′—B′ to the muscle, and the nearness of either A′ or B′ to one end of the muscle. As the distance of the electrodes from the muscle is increased all the phases are diminished and the already smaller elements of the deflection rapidly become too small to record. As a result of the overlapping of the effects from A′ and B′, and of the dropping out of phases which have become too small to record, the deflections usually obtained from such muscle preparations with electrodes in the position of A′ and B′ are triphasic when the electrodes are near to the muscle and diphasic when they are remote.

From these results we see that if we regard the strip X—Y as consisting of the active skeletal muscle, and the electrical field resulting from its activity as being set up in the surrounding conducting medium provided by the other structures of the limb in which this muscle is lying *in situ*, we may summarize concerning the deflections to be expected in this way: the deflections will be diphasic in form in all cases except where the electrodes are placed in intimate contact with the muscle, are well separated each from the other and from the ends of the muscle, and are in such a position that the wave of contraction or activity passes immediately beneath them both: in which case they will be triphasic.

In the section dealing with the form of the deflections making up the voluntary electromyogram it was stated (p. 345) that Wacholder had found triphasic deflections to be constant for the tibialis anticus. It is possible that the relatively superficial position of this muscle, which allows surface electrodes to come into closer contact with it than with most other muscles recorded, is sufficient to explain this result.

The results above described have been obtained from a parallel-fibred muscle strip, stimulated to contract at one end, so that a wave of contraction passes along the muscle from the end stimulated. In the case of voluntary contractions of intact skeletal muscles we are dealing, for the most part, with muscles which have in some degree a pennate arrangement of their fibres and in which the spread of the contraction is not entirely a function of muscular conduction but is probably the result of the intramuscular nerve filaments. In the case of the isolated muscle strip the moment at which any particular part of the muscle contracts depends upon its distance from the end stimulated. In the case of the intact, composite skeletal muscle it might be expected that the sequence in which the different parts of the muscle contract depends upon their physical distribution about the tendon through which their effect is exerted, and not upon their distance from any particular transverse plane of the muscle, e.g., the nervous equator.

That some parts of a muscle such as the quadriceps femoris are normally thrown into contraction before others has been shown by Golla and Cook [30], who find that when this muscle is voluntarily contracted a wave of activation seems to spread down the muscle distally. That this effect is not due to conduction in the intramuscular nervous filaments is considered by them as decided by the observation that the rate of spread is six times as slow as the rate of nerve conduction.

These authors find that when the two electrodes are either both proximal or both distal to the nervous equator, the current of action is diphasic and in an opposite direction in the two cases. When the electrodes are placed one on either side of the equator the current of action is triphasic, as a result, they believe, of "the interference of two diphasic electrical responses travelling in opposite directions" (p. 50). This interpretation is not tenable. For presumably in the other cases of the two electrodes placed toward one end of the muscle so that activity spreads first under one and then under the other, the diphasic form of the action current is regarded as being due to relative negativity of the first electrode with regard to the second, and then of the second with regard to the first. If it were other than this one would expect a polyphasic deflection. When the electrodes are placed one on either side of the nervous equator, on the supposition that a wave of contraction (negativity) spreads up and down the muscle from this plane, the effect of the wave spreading proximally should be a transitory relative negativity of the proximal electrode, that of the wave spreading distally should be transitory relative negativity of the distal electrode. We should thus expect the electromyogram to show a diphasic alteration in relative potential as a result of the fusion of these two monophasic changes. In no case could a triphasic current of action be anticipated. However, these results are capable of another explanation. It has been shown above that the conditions which favour the appearance of triphasic action currents include wide separation of the electrodes from each other and from the ends of the muscle, so that the active region lies wholly beneath them and not mainly to one or the other side. These conditions are more nearly fulfilled by the case in which the electrodes are separated to either side of the nervous equator than in any other position, and it is suggested that this, rather than the presence of a dual wave of activity, is the cause of the triphasic response so obtained.

III.—THE RELATION BETWEEN THE ELECTRICAL AND MECHANICAL EFFECTS IN MUSCLE.

Of the three associated phenomena which commonly characterize the activity of muscles—namely, shortening or tension development, metabolism with heat production, and electrical phenomena—it is the first which gives them their value in the intact organism and which may properly be regarded as their function. It is thus in terms of mechanical change that the galvanometer deflections must be considered. The electrical variations responsible for these deflections occur only in intact muscle in association with activity, i.e., shortening or tension development. Whether the three phenomena mentioned above are all concomitant expressions of some underlying fundamental change, or whether any one of them stands in casual relationship to the others, will have in due course to be considered.

That the electrical variations observed in the locality of a contracting muscle are not adventitious to the muscle function in the same sense as is the heat liberated on contraction, is indicated by the constancy with which apparently normal mechanical, metabolic and electrical changes are set up in response to electrical stimulation of the denervated muscle. We may now consider the temporal and quantitative relationships of the electrical and mechanical changes.

The relation in time.—Einthoven and Hugenholtz [19], finding that there was no interval between the appearance of the electrical and of the mechanical change, concluded that there were but different results of the same process. A similar conclusion was reached by Arbeiter. Fulton has repeated these observations with more exact methods and finds that the electrical precedes the mechanical change in the skeletal muscle of the frog by about 1·5 sigma [27]. A much longer value is given by Kleinknecht [46] who reports that cooling of the muscle may increase the period up to three times its original value. Fulton has also found that the size of the electrical change is proportional to the initial heat liberated. These results indicate that the electrical change precedes the mechanical change by an interval which suggests that it is an index of those processes of which the tension contraction effect is an immediate result.

In the case of the ordinary phasic twitches of skeletal muscle the electrical is of much shorter duration than the mechanical effect, and while in tetanus a plateau of maintained tension may result from complete fusion of the mechanical contractions, the electrical responses to stimulation always remain distinct and separate. It is only in the long drawn-out action currents associated with some forms of tonic contracture in striated muscle that any approximation of duration of electrical and mechanical responses can be found (Lee [47], Bishop and Gilson [10]).

The relative size of electrical and mechanical responses.—In a parallel-fibred muscle increase of submaximal stimuli leads to increase in size of both effects, due to the activation of more and more muscle fibres. When maximal tension development is reached further increase in the strength of the stimulus does not lead to any further increase in amplitude of the electrical variation. With repeated just-maximal stimuli both effects diminish as fatigue appears. Fulton finds [25] that they run parallel courses in their decrease to become extinct together. Beritoff [9] on the other hand finds that neither their courses to extinction nor their recovery rates after cessation of stimulation are parallel. But he used the gastrocnemius preparation from a frog, and Forbes, Ray and Hopkins [22] have explained the prior extinction of the mechanical effect found by him in terms of the obliquity of the fibres in this muscle.

In the unfatigued muscle-fibre it is to be expected that the electrical effect will be of constant amplitude and that it will give a true indication of the functional mechanical activity of that fibre however this is stimulated, e.g., voluntarily or reflexly.

IV.—The Relation of Galvanometer Deflections to Activity of the Central Nervous System.

As we have seen, the familiar electromyogram of voluntary muscular contractions obtained by the use of two distant electrodes and a string-galvanometer consists of a number of deflections of varying sizes and differing rates. But, as Hoffmann [38] has pointed out, we cannot safely infer anything as to concomitant central nervous activities from records of electrical phenomena in muscle obtained in this way. It is true, as will appear later, that records from electrodes arranged so as to "tap" individual muscle fibres do provide information as to the conditions of motor-nerve innervation and thus allow of conclusions as to the activity of nerve centres. For the present, however, we are concerned with the older type of electromyogram obtained by distant electrodes which tap a whole muscle mass.

In Chapter III, reasons were advanced for believing that the electrical variations under consideration were entirely an expression of muscular activity, and there are no grounds for suggesting that deflections of one size and rhythm are contributed by nervous impulses of a corresponding rhythm, and that those of another rate are arising in the muscular responses to those impulses. All arise in the muscle and thus all stand in the same relation to the activity of the motor-nerve neurones. The size of each deflection will depend mainly upon the number of muscle units engaged.

Two assumptions have been made with regard to the relation between the frequency of motor-nerve impulses and the galvanometer deflection rate. One assumption, that the muscle possesses an inherent rhythm at which it responds to motor-nerve impulses at a higher rate, has been carefully examined and found insufficient by Adrian [1]. The other, that the muscle shows a repetitive response to a slower rate of innervation, is based upon equally unsatisfactory grounds (Wacholder).

Although the result of experiments designed to show simultaneity of activation of different parts of the same muscle (Wacholder) or of neighbouring muscles (Altenburger and Forster) must be taken with reserve in the absence of strict control as to the origin of such action currents, simultaneous records of motor-nerve impulses and muscular contraction (as taken from the phrenic nerve and diaphragm by Dittler and Garten [17]) give strong support to the view above stated that the muscle contributes nothing in the way of inherent rhythm to the frequency of the deflections.

Since the amplitude of the galvanometer deflection is determined by the number of muscle units active, if each unit were innervated by a separate and distinct path from the central nervous system we should be able to decide from the frequency and amplitude alone just how many lower motor neurones were active at any given moment and at what rate. This is, however, not the case. One motor neurone may activate several muscle units, or a single muscle unit may derive its innervation from more than one motor unit. The second of these possibilities has been shown to be unlikely in the case of the frog and the rabbit (Fulton [26]), for which animals it was originally suggested, and it is improbable that it occurs in man. The former suggestion is almost certainly true. The number of nerve-fibres in a motor nerve is far smaller than the number of muscle fibres in the muscle which it innervates, so that it is clear that each nerve-fibre must be capable of activating more than one muscle-fibre, in much the same way as Adrian has shown to hold for the afferent nerves from skeletal muscle where several tendon end-organs are connected with each afferent fibre. If we could assume further that activity of a nerve-fibre always entails contraction of all the muscle-fibres which it innervates then this complication could be disregarded and the units of electrical field production shifted from the individual fibre to the composite unit. But it will be later shown that such an assumption is not valid.

The central nervous discharge may be varied only in certain ways, e.g., in respect of the number of neurones involved, the rate of the impulses in each neurone, and the time relations of the activities of the various neurones.

In view of the relatively short refractory period of the peripheral nerves it is probable that they do not contribute anything in the nature of an inherent rhythm modifying that of the central motor innervation : but that they simply pass on unaltered the train of impulses which results from voluntary or reflex excitation of the anterior horn-cells. It is known that repeated rhythmic stimulation of an afferent nerve will lead to reflex motor discharges which reproduce faithfully the stimulating rhythm up to rates higher than those which are met in the normal electromyogram, so that it is probable that the source of any rhythms present during voluntary activation must be sought at a higher level than the lower motor neurones. The results of rhythmic stimulation of the cortical motor centres have not given unequivocal evidence in favour either of a central or of a peripheral dominant rhythm. Keller [44] found that the rate of stimulation of the cortex was followed strictly by the electrical discharge from the muscle up to 170 stimuli per second. Cooper and Denny Brown [15] working with monkeys found a similar parallelism from 160 to 180 per second, and Plattner [50] found it in dogs between 80 to 200 per second. However, Hoffmann [39] found that in dogs only rates between 40 and 50 per second were accurately followed, at lower rates the muscle responded at a double or treble frequency and at higher rates the frequency was halved. The first experiments suggest that if there is a dominant rhythm within the limits given then it is probably not cortical in origin, the second suggests that the cortex tends normally to discharge at 50 per second, a rate which has been much in favour as a characteristic of normal voluntary electromyograms.

It is of interest here to examine the possible significance of this 50 per second rhythm. It has been subscribed to by so many observers and confirmed in so many different ways that it cannot be due to any particular form of recording, but must represent the tendency for periodic large alterations in the electric field at this rate, i.e., for a tendency to synchronization of the muscle elements at this rate. That it is a synchronization effect follows clearly from the fact that it is only by synchronization of the smaller elements that larger deflections can be produced and also from the fact that in those records or in those parts of any one record in which this rhythm is best marked the secondary waves due to elements out of phase are least conspicuous.

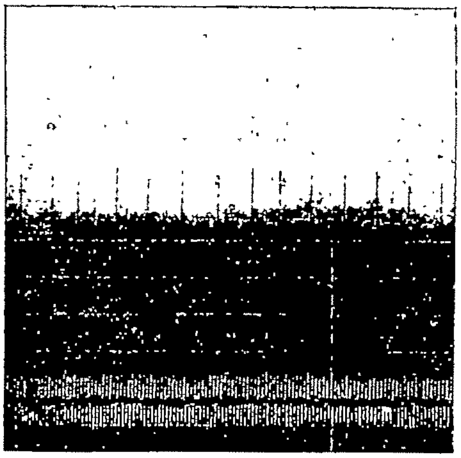


FIG 1.

From a muscle such as the triceps of the arm during voluntary activation, using needle electrodes (Adrian and Bronk [2]) and the Matthews oscillograph, records such as those shown in fig. 1 are obtainable. With the slightest degree of voluntary effort a series of deflections of equal and small amplitude are obtained; and evidence has been given elsewhere (Pritchard [52]) for regarding these as coming from the individual muscle units. With higher degrees of effort there is found not only an increase of rate but an increase of amplitude: the intermediate stages of fusion of individual units can be clearly traced upon intermediate records. If the record of a strong voluntary contraction is measured it is found that the larger deflections, which are quite irregularly spaced, occur at the rate of 45 to 48 per second, upon a background of very many smaller deflections, these deflections are due to the same periodic electrical changes which give the large deflections —" A" or primary waves—of the string-galvanometer record and Piper's "50er Rhythmus." It was suggested in the same paper that the maximal number of motor units which could be simultaneously activated during a voluntary effort might be a function of the neuronic connections " either in the peripheral nervous pathway or at a higher level."

To summarize this view of the relation between electromyographic deflections and central nervous discharge, it is suggested that the type of record obtained with the string-galvanometer and two independent distant electrodes gives no direct clue to the rate of motor impulses in the peripheral nerve-fibres, in view of the complexity of the muscle mass, all of which contributes to an electrical field which is "tapped" in comparatively distant regions. Thus it is impossible to separate the responses obtained from functional units one from the other, but the rates of deflection so obtained are determined wholly by the rates of discharge along the lower motor neurones. Records obtained from more strictly localized intramuscular electrodes do enable us to infer with a high degree of probability the rates of discharge in certain cases. The 50 per second rhythm, which has been held to characterize the electromyograms of voluntary movements and for which many different origins have been suggested, is probably a function of the relation between the number of motor-fibres and the number of muscle units which they supply, and does not represent the inherent tendency to discharge at that rate either of the muscle or of any part of the central nervous mechanism.

V.—The Influence of Fatigue upon the Action Currents of Voluntary Movements.

Three changes have been recorded affecting respectively the amplitude, the form and the frequency of rhythm of the galvanometer deflections. The fall in total frequency of the large waves from 50 per second to 35 or even 20 per second noted by Piper, has been generally confirmed (Altenburger [3], Altenburger and Guttmann [4], Gregor and Schilder [31], Cobb and Forbes [13]). An increase in frequency has not been observed, but some (Dittler and Garten [17]) who have counted the total oscillations and not the larger waves alone, have come to the conclusion that the diminution in frequency of the former is apparent only, and is due to the fact that some oscillations become too small to be detected.

In almost all cases the observed drop in frequency is associated with an increase in amplitude of the larger waves. Altenburger and Guttmann [4] have established from their records a reciprocal relation between frequency and amplitude as holding good in the earlier stages of slowly fatigued voluntary movements. The interpretation of this relationship is helped by the observation that associated with it there is a diminution or absence of the "Nebenzacken" or secondary wavelets leading to relative quiescence of the galvanometer between the larger waves (Piper [49], Gregor and Schilder [31], Altenburger [3]). This suggests that with the onset of fatigue the motor cells of the cord tend to fire off simultaneously in volleys so that there is an increasing degree of synchronization of the different muscle units: a conclusion reached by Bornstein and Sanger [11], Fulton [24] and Haas [34]. The further observation of some workers (Piper [49], Altenburger [3]), that the large waves are more drawn out, i.e., of increased duration—although this is not found by others (Cobb and Forbes [13], Gregor and Schilder [31])—may be explained as due to the incomplete volleying of the neuromotor units giving incomplete fusion of the muscle units, whose slight temporal dispersion leads to a prolongation of the summated electrical action currents.

Altenburger [3] and Altenburger and Guttmann [4] have distinguished between changes occurring in loaded and in unloaded muscle and in fatigue attained rapidly or gradually. Thus they found that the increase in amplitude of the oscillations is found only in loaded muscle and that late in fatigue it gives way to an increase in duration, the synchronization of different muscle elements becoming less perfect. When the volleying of impulses becomes still more complete, or when a further stage of approximation of the moments of discharge of greater numbers of neuromotor units is reached so that the summated effects from different groups of muscle units tend to be thrown together, the galvanometer record shows grouping of the deflections corresponding with periodic outbursts of approximately synchronized activity. Bornstein and Sanger [11] have associated this grouping or volleying of higher degrees of fatigue with the development of fatigue tremor. The greater the degree of fusion or volleying of the impulses the larger will be the number of muscle units which become active simultaneously and the more pronounced will be the tremor.

It appears, therefore, that when voluntary activity of the same muscle is prolonged there develops a tendency for volleying of the motor discharge with increased synchronization of the different muscle units, leading to action currents of greater amplitude and diminished frequency, and finally to a degree of fusion which results in tremulous maintenance of tension by the whole muscle.

These being the changes in the electromyogram in fatigue it is natural to inquire as to the mechanism of their production. About this question there is at present less agreement. It has been shown (Pritchard [52]) that the volleying of impulses during fatigue of voluntary contractions is exactly similar to that which may be seen to characterize any severe muscular effort which leads to a tremulous contraction; and this from the outset of such an effort and before the normal fatigue mechanism can be regarded as playing any part. It is, therefore, reasonable to look within the central nervous system for the mechanism productive of both fatigue and effort tremor. The changes occurring in the muscle itself during fatigue do not provide an explanation. It is probable that the muscle mechanisms have a sufficient reserve to render them relatively unfatigued under physiological conditions, including those of voluntary movement fatigue (Guerra [32]). It has been shown (Beritoff [9]) that when a muscle is fatigued experimentally by repeated stimulation of its motor nerve the current of action is affected less easily and to a smaller extent than the power of contraction—indicating a relatively greater resistance to fatigue which is paralleled by the more rapid and earlier complete recovery of the action currents after cessation of the motor-nerve stimuli. Beritoff explains this effect as due to the fact that the electrical effect is associated with excitability ("erregbar Substanz") and not with the acid breakdown which results in the mechanical change. Fulton [26], who holds that action current and contraction run a parallel course towards extinction during fatigue, points out that since the accumulation of contraction catabolites in the muscle results in diminution of the action current, the increase in amplitude of the oscillations seen in the fatigue electromyogram cannot be referred to an increase of electrical effect from each muscle unit active, but can only be explained on a basis of synchronism of their innervation.

v. Weizsacker [76] refers the diminution in frequency and increase in amplitude to fatigue of the proprioceptive nerve-endings in the muscle, holding that the central nervous system tends to discharge from its motor neurones with a slow automatic rhythm, and that in all normal voluntary movements this rhythm is broken up by the interference of proprioceptive impulses received from the muscle innervated. With fatigue of these proprioceptive nerve-endings and the consequent diminution of their effect, there ensues a nearer approximation to the slower automatic rhythm of the central nervous system. Against the suggestion that such changes may result from a fatigue of the central nervous discharge, he draws attention to the results of Hoffmann [39] who found no evidence of fatigue in the stretch reflexes after 10,000 repetitions in three minutes. But this provides an equally sound reason for rejecting the notion of fatigue of the proprioceptive nerve-endings, since the integrity of the stretch reflex is as much dependent upon their cooperation as it is upon the motor discharge.

The increase of the tendon-jerks normally associated with voluntary fatigue indicates that the proprioceptive stretch reflex mechanism is made hyper-excitable rather than diminished in activity and accords with Fulton's suggestion that an accumulation of catabolites in the muscles may make the proprioceptive nerve-endings more readily responsive. This hyper-activity of the proprioceptive reflex mechanism will give a relative increase in the reflex component of voluntary innervation and a relative diminution of the cortical component leading to diminished "temporal dispersion" (Fulton [24]), i.e., increased synchronism, increased amplitude of the action currents, and mechanical tremor. The observation that the rates of clonus and of fatigue tremor are identical is adduced in support of this view. It has been shown that a very strong isometric voluntary contraction of a group of muscles is frequently tremulous from its beginning and the electromyogram shows a characteristic tremor; this suggests that the majority of the effective muscle units have been thrown into synchronous activity. When the same group of muscles is fatigued by repeated voluntary contraction with a very light load (the muscles being allowed to shorten and extend fully with each effort), shortly after fatigue is noticed there appear changes in the myographic and electromyographic records which are strictly comparable to the above, i.e., shortening and lengthening become tremulous and intermittent and the electrical discharge becomes volleyed in the same way. There can be no adequate reason for regarding the changes occurring in these two sets of circumstances as being different in origin or nature, and the terms "effort tremor" and "effort syndrome" may be used in respect of either. They both have a sense of strenuous activity as the mental counterpart of the physical changes, and it has been pointed out in the same paper (Pritchard [52]) that the tremulous movements of paralysis agitans are indistinguishable from those of isotonic and isometric fatigue in respect of all three characteristics.

It is convenient to have some term which will express the occurrence of this group of phenomena modifying voluntary movements. The term *effort syndrome* has been here suggested and will be used to denote that type or that phase of voluntary movements, accompanied by a sense of (strenuous) effort, in which the mechanical shortening is intermittent or the tension maintenance discontinuous, and the electromyogram is of the grouped or volleyed type. The group frequency of the electromyogram is in any one case identical with the intermittent frequency of the mechanical contraction, the one being a record of periodic outbursts of activity which determine the occurrence of the other.

In the case of repeated isotonic movements and of paralysis agitans, induced fatigue in the former and chronic fatigue in the latter might lead to fatigue of the peripheral mechanisms of contraction and to the accumulation of catabolites which exercise a secondary effect upon the proprioceptive nerve-endings. But such a sequence of events can clearly not be held responsible for the alterations in the efferent discharge producing the effort syndrome in the case of a suddenly initiated, strong isometric movement.

Again, the excessive stimulation of the proprioceptive end-organs which probably occurs in a very strong isometric contraction might be regarded as providing an explanation for the effort syndrome in this case, but the development of an excessive tension does not take place in the case of unloaded shortening and lengthening movements and, therefore, cannot account for the appearance of the effort syndrome in either isotonic fatigue or in paralysis agitans. Further, it has been shown by Adrian [1] that such excessive stimulation of the tendon organs leads to their well-marked fatigue with diminution in their rate of discharge. We have seen above that there are serious objections to the notion of fatigue of proprioceptive mechanism as underlying these synchronization effects and that their hyper-activity would provide a better explanation.

We must, therefore, conclude that there is no adequate explanation of the voluntary effort syndrome in terms of peripheral changes such as an alteration in the muscle or in the afferent impulses received from it. It remains to be determined whether there is any explanation forthcoming from consideration of the central nervous mechanism on the purely motor side.

The change in the form of the electromyogram which results from the fusion of asynchronous elements into synchronous groups is clear cut. It results in a series of separate deflections of uniform amplitude occurring at the rate of 45 to 48 per second. It is due to the use, by the innervation mechanism, of a new effector unit; the composite group innervated from a single or from intimately related motor neurones.

The further change, occurring in fatigue, which results in the grouping together of these larger deflections is by contrast the consequence of a process which is not nearly so definite: the groups, as such, are distinct but the further fusion of deflections is never complete. The individual deflections, although grouped, still occur at the same average rate. These characteristics suggest that the grouping or volleying effect is the result of some periodicity of action of a central multi-fibre mechanism having a natural frequency which is only elicited under abnormal conditions.

The mechanism which has been shown to account satisfactorily for the first stage of synchronization of the motor impulses, i.e., that from individual units to composite units, may be operative wherever any single proximal centrifugal pathway exerts control over several distal centrifugal paths. Since this condition obtains at higher levels in the nervous system it might be expected that the further degree of approximate synchronism of the larger units results from a similar mechanism higher up the motor paths. It might for example take place at the level of transmission of motor innervation from the pyramidal fibres to the anterior horn cells, or at the level of influence of the cells of the motor cortex by some other region of the cerebrum. There are, however, several reasons why it is improbable that such a mechanism comes into play at these levels.

In the first place, the two steps towards temporal fusion of deflections, as above indicated, are of different types. The peripheral mechanism (a function of the lower motor neurone and muscle-fibre) is one frequently called into play in all movements of moderate intensity. It results in a type of innervation which is still completely dispersed and aperiodic, giving still a smooth contraction and sustained tension development. The suggested central mechanism is one which provides a type of action which characterizes abnormal efforts, whether in disease, fatigue, or over-exertion. It results in a form of discharge which is uneconomical; the contraction is intermittent and the tension discontinuous. In normal persons the primary synchronism of individual units into larger units invariably precedes the secondary synchronism into groups. For this to obtain the frequency of the impulses in the most central paths requisite to synchronize all the intermediate paths must be greater than that sufficient for synchronizing all the individual muscle-fibres into a secondary muscle unit. Therefore, if the central and peripheral mechanisms are of identical type, the first stage of fusion into larger muscle units must always precede the second stage of grouping into volleys. But this is not the case in either isotonic fatigue or in paralysis agitans, where volleying and tremor can take place with the motor units still acting separately.

The groups of deflections in the effort syndrome indicate outbursts of activity producing a tremulous contraction which involves the whole or most of the muscle, so that for the grouping to be the result of a mechanism similar to that already outlined would take us up to a level at which a single neurone, or a multifibre but synchronous motor pathway is at work providing all the excitatory innervation. Such tremor cannot be contributed by anything less than the whole motor mechanism at some level. It must mean that at such a level the mechanism, although still composite with regard to the number of pathways through it, is imposing upon the impulses which it transmits a secondary regular rhythm. It must be a mechanism which is capable of responding aperiodically in normal circumstances, but which under certain conditions contributes that secondary rhythm which results in its breaking up a continuous stream of impulses coming to it into a discontinuous stream of impulses passing from it, i.e., in converting a steady incoming stream of impulses into an intermittent outflow.

In the field of applied physics there are several other similarly related systems which show the same type of action, i.e., the conversion of a continuous into a discontinuous discharge by virtue of an inherent periodicity, and it is instructive to examine these further.

The ordinary whistle when blown into gently transmits merely a rush of air; as the speed with which the air passes through is increased a value is reached at which a note is elicited, i.e., at a certain pressure of air the natural period of the whistle is excited and oscillations are set up. Perhaps more strictly parallel if less familiar is the behaviour of fluid flowing through a circular pipe. At low velocities the lines of flow are axial, that part of the fluid flowing down the centre of the pipe having the greatest velocity and that in contact with the walls being virtually at rest. As the pressure of input and speed of flow are increased, a value is reached at which the above conditions are no longer present. Vortex flow is substituted for axial flow; the fluid rolls over the sides of the pipe. Vortex waves are set up and the discharge becomes oscillating. The rate of flow at which this takes place depends upon the pipe as well as upon the fluid, and has been empirically expressed in terms of the viscosity and density of the fluid and the radius of the pipe.

An example of an oscillating system in another field of work is provided by an electric circuit which contains a condenser and an inductance; the frequency of oscillation of such a system may be shown to be a function of the capacity of the condenser and of the inductance.

It may be argued that in these examples the parallel is imperfect because the input is truly continuous, whereas this is never the case with central nervous innervation. Yet if we examine other systems to which the objection cannot be raised, we find that the same type of relation between the critical rate of input and the properties of the system holds good. Thus if a stretched wire is periodically displaced transversely at one point and as often released, a series of waves travel along the wire in both directions from the point displaced, these waves having a distance apart dependent upon the frequency of displacement. As this frequency rate is progressively increased a stage is reached at which the natural frequency of the wire is called out and stable oscillations of a different form are set up. This frequency is expressed in terms of the tension in the wire and the mass per unit length. The The above vibrations are transverse. Longitudinal vibrations similarly set up in any suitable medium such as a gas find a similar frequency in terms of the modulus of elasticity, and the density of the medium.

Taking each of these examples of oscillatory system, we find that tho essential properties upon which its characteristics depend, and in terms of which that critical input value which elicits an oscillatory discharge is expressed, are two in number and invariably of the same physical dimensions. One property is that of inertia or akin to it, and the other of elasticity, i.e., one limits the immediate effect of an impulsive stimulus or disturbing force and the other tends constantly to restore the condition of quiescence or equilibrium.

Thus in the electric system the inductance corresponds to the lag or inertia and the capacity to the elasticity. In the fluid system the viscosity represents the inertia, and the density the resistance to compression or tendency to re-expansion. In the stretched wire the mass per unit length determines the inertia which limits displacement and contributes the momentum of overthrow, and the tension in the wire determines the restoring force pulling the displaced elements back into line.

These two properties, one akin to inertia and the other to elasticity, endow the system in which they occur with the oscillatory characteristics which it shows. If, therefore, the central nervous mechanism which mediates the motor discharge between the cortex and the muscle, proves on closer examination to behave in its other activities as well, in such a way as to lead us to ascribe to it properties having similar characteristics as inertia or momentum and as elasticity, we may conclude that it contains within itself those properties the combination of which is both essential and sufficient for the production of an oscillating or volleyed discharge.

Such a mechanism cannot be determined by the physical property of the muscle itself because this varies so considerably in the different conditions in which the tremor effect can be observed. It is probably not at the level of the cortex because, as Fulton has pointed out, the rate of effort tremor and of clonus are identical under comparable conditions, so that it is probably a mechanism which is shared by both voluntary and proprioceptive reflex activities. It cannot be anywhere along the lower motor neurones because the whole muscle is involved. We must conclude, therefore, that if it exists at all it must be somewhere along the course of the reflex pathway central to the motor neurones and yet on the efferent side of the reflex arc.

In a subsequent paper it will be argued that a mechanism having the properties of mass and elasticity and situated in this position will adequately account for the observed facts of spinal reflex behaviour in respect of excitation and inhibition. These facts have been examined and their interpretation attempted in terms of such a "ballistic model." The conclusion is reached that not only is the behaviour of the effector mechanism, under conditions of reflex excitation, also compatible with the presence of a nervous centre acting in a certain way, paralleled in the field of mechanics by a system having these properties, but that it can be more completely interpreted in terms of such a system than in terms of any other hitherto suggested.

VI.—PATHOLOGICAL CONDITIONS.

Myasthenia gravis, paralysis agitans, lower motor neurone lesions, spastic conditions, tabes dorsalis, reflexes in "spinal" man, involuntary movements, chorea, convulsive states and contractures.

Myasthenia gravis.—In 1914 Athanasiu and Harrison [6] reported two observations upon the voluntary electromyogram in myasthenia, i.e., that the action currents were smaller than normal and in the same direction as those of resting muscle. By contrast they reported that the direction of the action currents in normal persons during voluntary activity was the reverse of those present in resting muscle. This normal or pathological alteration in current direction has not been found by any other workers and is probably a consequence of their electrical circuits, but their diminution in the amplitude of the deflections has been since confirmed by Herzog [36] in 1917, Schaffer and Brieger [63] in 1922, and Woolf, Kleitman and Cobb [77] in 1928.

Herzog found that this was the only particular in which the electromyogram was abnormal and made the important additional observation that such patients may be fatigued to a standstill without any subjective feeling of fatigue. Woolf, Kleitman and Cobb found that the only change was one of amplitude. As fatigue advanced the frequency of the deflections remained unaltered and the amplitude, small even at the beginning, increased during the first bout of work and later slightly diminished. In contrast, when a healthy muscle was fatigued the frequency became less and the amplitude greater. Artificially induced venous stasis had no effect on the electromyogram.

Both Herzog, and Schaffer and Breiger examined the effects of electrical stimulation of the muscle at its motor point. The former found that a single stimulus resulted in many contractions, with a single action current followed by many small wavelets; the latter authors found that each stimulus gave a diphasic action current but that faradism gave a series of abnormally small deflections. Both found that the latent periods of the tendon reflexes were unaltered. They concluded that the defect lay in the muscle itself. Woolf, Kleitman and Cobb placed the essential lesion peripheral to the anterior horn cell.

The sudsidiary observations made by these authors are of great significance with regard to the site of the defects leading to the characteristic symptoms of the disease.

Herzog [36] noted the absence of a sense of fatigue even when voluntary movements had become impossible, and the absence of normal fatigue changes in the electromyogram. Woolf, Kleitman and Cobb [77] confirmed both these observations and also noted that more vigorous contractions, when these were possible, showed a greater tendency towards rhythm of their electromyogram than weaker contractions. They particularize the departure from the normal fatigue picture as showing an absence of the usual increase in amplitude and the decrease in frequency; changes which have been shown to result from a greater degree of synchronism of the muscle units and a greater degree of volleying of the innervation impulses. It is clear, therefore, that we may summarize the findings in this disease as consisting of an absence of both the subjective feeling of fatigue and the increased synchronism of the innervation impulses to the muscle units, i.e., a failure of the normal voluntary effort syndrome which has been shown above to be associated with a central nervous mechanism rather than with the peripheral muscular or neuro-muscular apparatus.

Paralysis agitans.—Bornstein and Sanger [11], and Hoffmann Hansen and Weizsacker [40] reported that action currents are present in the resting limbs of patients suffering from Parkinsonian rigidity apart from any static tremor. These results are not confirmed by Gregor and Schilder [31], and Pritchard [52], who found that the resting limb was free from electromyographic signs of activity.

Hoffmann, Hansen and Weizsacker [40] further found that passive movements impressed upon the rigid limb without active co-operation or resistance result in periodic waves of increase of the electrical activity present in the quiescent limb. Pritchard's records of such passive movements show a series of notches upon a gradually shifting base line, these notches corresponding with the separate stages of the intermittent resistance felt in manipulation of the limb; the notches are themselves due to electrode shift at each transitory interruption of movement and each is immediately preceded by a small outburst of electrical oscillations, the curve being otherwise free from signs of action current.

Gregor and Schilder [31], 1913, showed that the static tremor corresponded to a series of tetanic contractions each of which yields two to four galvanometer deflections ("foot tremor"). In the following year Bornstein and Sanger confirmed these results. They found groups of three to five big waves at the rate of 50 to 60 per second, the groups recurring at intervals of $\frac{1}{5}$ per second with no "Nebenzacken." This rate they held to be characteristic of tremor of central nervous origin, tremor of partly myogenic origin having less frequent action currents. Rehn [58], 1922, reported that the tremor was associated with groups of large waves at the rate of 6 per second, each group containing two to three waves. Small waves at the rate of 45 per second were also present. Cobb [12], 1923, found the tremor rate averaged 5·8 beats per second, each beat was associated with a group of 2 to 4 deflections at the rate of 46 per second. Between these groups the galvanometer was not at rest but gave smaller deflections at the rate of about 70 per second.

All these observers found voluntary movements to be associated with a series of action currents which tend to be grouped into volleys. Bornstein and Sanger [11] found these volleys to be absent at the beginning of such movements but to appear after about 1⅝ second. The only difference which they found between static tremor and voluntary movement records were in respect of the amplitude, which was greater in the latter, and of the "Nebenzacken" which were absent in the former. Rehn [58] confirmed the absence of grouping of impulses at the beginning of contraction and its reappearance after contraction has progressed for a time. Pritchard [52] found in a series of patients with varying degrees of severity of affection, all stages of transition between the normal electromyogram and one in which well-marked volleys occurred at the rate of 6 to 8 per second. It was shown that such volleying is maximal when a constant tension is being actively maintained at a given degree of shortening, and disappears during stages of tension increase or progressive shortening to reappear whenever the tension is again kept constant. This disappearance of volleying with increasing tension (shortening) was not found to nearly the same extent during periods of decreasing tension (lengthening). It was shown that the tremor of movement and volleying of action currents were not, as such, signs of disturbed nervous function but occurred in normal persons in certain circumstances. They appeared in all records from patients suffering from paralysis agitans at a level of less effort and smaller tension: the difference between the electromyograms in this condition and in normal healthy persons being thus quantitative rather than qualitative.

The electromyogram in lesions of the lower motor neurone.—Richter and Ford [60] have studied the voluntary electromyogram in cases of anterior poliomyelitis, progressive muscular atrophy and syringomyelia, They came to the conclusion that such records were characterized by the following changes. The frequency of the primary waves is reduced, and may be as low as 5 to 10 per second; while the muscle is being stretched this increases up to the normal 50-per-second rate, but again decreases when the stretch is maintained. There are sometimes two rhythmic series of deflections each constant in rate and appearing or disappearing independently of the other. The amplitude, which is usually constant, is increased and there is a noteworthy lack of proportion between the large deflections and the feeble contractions. The duration of each deflection is short, $\frac{1}{120}$ per second as compared with the normal $\frac{1}{80}$ per second. There are no secondary waves and a remarkable freedom from "Nebenzacken." It should be noted that these authors consider the latter to be due to action currents of the same origin as the primary waves and arising from elements out of phase with those which fuse to give the larger deflections. They suggest that when the reflex arc is only partially interrupted on the motor side, voluntary movement still being possible, it may be impaired to such a degree that although the tendon responses are abolished, the proprioceptive control of the innervation rhythm is maintained. Yet they hold that simple interruption of this reflex arc alone does not give the slower rhythm, for the frequency can vary in appropriate circumstances from 5 to 50 per second, the transition from one rate to another is smoother than in tabes dorsalis, and although the proprioceptive arc is interrupted in both cases the rhythm is different.

They consider that in one of their cases they were dealing with a "lesion of the motor horn cells so widespread as to leave only a few fibres intact," so that the low frequency was due to an insufficient number of impulses passing through the motor horn cells to produce an average strong contraction and thus the higher frequency of proprioceptive impulses." This they believe accounts also for the simplicity of the waves, their narrow base or short duration and the freedom from "Nebenzacken." They contrast these results with the normal electromyograms from cases of muscular dystrophy in which "what remained of the muscles could be brought into full tension" so that the usual high frequency of primary waves resulted.

The electromyogram in spastic conditions. Resting muscle.—Many investigators have reported the presence of action currents in the spastic muscles of a limb when this is fully supported and no effort at contraction is being made. This observation was made by Gregor and Schilder [31] using the calf muscles, which gave a series of small deflections in groups at a rate of 30 per second. Bornstein and Sanger [12] recorded from the biceps of the arm a similarly discontinuous stream of irregular action currents at a rate of 30 to 35 per second. In 1921 Rehn [56], using needle electrodes, found alternate periods of quiescence and activity in the records from resting muscle of a case of disseminated sclerosis, and Hoffmann, Hansen and von Weizsacker [40] obtained similar records from the contractured limbs of a case of spinal compression and from the calf muscles of a child suffering from cerebral diplegia. Rehn [56] in a similar diplegic case records a continuous stream of tetanic "Dauerinnervation" which he considered to be characteristic of spasticity of cortical origin as contrasted with the discontinuous volleys of cases of spinal damage.

Passive movements of spastic limbs.—Gregor and Schilder [31] obtained curves from spastic muscles when passively stretched which were distinguishable from those of clonus only by the higher frequency of deflections (25, 33 per second). von Weizsacker [76] found that a perfectly normal electromyogram was given by passive stretch, and together with Hoffman and Hansen showed that the action current discharge persisted at a higher rate than in resting unstretched muscle, for long after passive movement was complete.

Voluntary movements of spastic limbs.—Samkow [62] (1912) found that voluntary movements in spastic cases were accompanied by regular action currents of longer duration ($\frac{1}{12}$, $\frac{1}{30}$ per second) and diminished frequency (11, 12 per second). Gregor and Schilder [31] found that in spastic limbs which were still under voluntary control two rhythms competed for command of the action currents. The more normal, rapid rhythm predominated in cases of slight severity, except at the beginning of movement; the slower rhythm became more prominent as the spasticity increased. The beginning of any movement was characterized by small groups of deflections at the same rate as the clonus, but during the course of the movement they were spread out and at the rate of 30 to 40 per second. Later still or with greater effort the slower rhythm returned until the complete clonus rhythm was re-established.

Bornstein and Sanger [11] confirmed these results in the following year; their groups of six, seven or eight action currents occurred only at the beginning of movement, after this the normal curve was present. From the fact that each action current lasted 0·03 second they concluded that the conduction time through the muscle was increased.

Gregor and Schilder [31] found that a tendency towards grouping of the deflections was present during voluntary movements in a case of flaccid hemiparesis; this suggests that the phenomenon is not entirely a result of increased reflex excitability and proprioceptive interference with the innervation rhythm.

Tabes dorsalis.—Gregor and Schilder [31], 1912, found that the electromyogram was altered in cases of tabes dorsalis only when the condition was advanced; the characteristics were then a diminution in frequency, an increase of the duration and considerable variation in the amplitude of the individual action currents. In addition, the intervals between the large deflections of the galvanometer were free from secondary waves and there was found to be an inverse relation between the action current frequency and the amplitude.

In 1921 von Weizsacker [76] published a detailed examination of several patients suffering from tabes dorsalis. Certain characteristics of the electromyogram were common to all his cases, others varied from case to case. Thus he described the typical "klare Bild der vergrosten, zackenarmen, verlangsamtern Ataxierhythmus" as occurring in all severe cases, but not until a high grade of ataxy was present. In one case no action currents were detected either in resting muscles or in those passively stretched, in another the action currents present at rest were increased by passive movements. He describes a clear difference between the electromyograms of isotonic and isometric contractions. In his first case the amplitude was inconstant but increased and the rate was diminished (15 to 18 per second) with intervals free from secondary waves. Isotonic movements were associated with a greater increase in amplitude; isometric movements with a greater decrease in frequency. In his second case, a patient with far less ataxy, the isometric record was normal but that of isotonic movements showed a degree of abnormality slighter than that present in the more severe case, i.e., the rate was not so much diminished and secondary waves were present in the intervals. In a third case isometric contraction of the knee flexors gave deflections of increased amplitude at 30 per second with no secondary waves; the extensors gave the same picture but for the presence of a few secondary waves.

Richter and Ford [60], 1928, reported very different results. They found that patients with a slight degree of ataxy gave electromyograms in which the primary waves were less frequent and secondary waves were prominent. Records from those more severely affected showed no primary waves but small secondary waves of irregular frequency. They conclude that interruption of the reflex arc alone does not yield a slow rhythm, because although the arc is broken both in tabes and in affections of the anterior horn cell the electromyograms from these two cases are quite different. Their results fit in well with Fulton's generalization that "encephalization involves temporal dispersion," i.e. that relative predominance of the proprioceptive reflexes leads to greater sychronization; for here, diminution and loss of the proprioceptive impulses have led to decrease and exclusion of the primary waves, with prominence and finally isolation of the secondary waves.

v. Weizsacker [76] holds the other view, that the central nervous discharge in tabes is of a slow, simpler (vereinfachter) rhythm unmasked by liberation from the dispersive action of the proprioceptive impulses which are normally present but lost or impaired in tabes.

It is certain that the damage sustained by the nervous system in uncomplicated but severe cases of this disease is not limited to that at the root-entry zone which leads to the loss of deep afferent impulses. There are many clinical reasons for supposing a more extensive impairment of function involving other central nervous mechanisms, and it is probably to a disturbance of motor discharge apart from the secondary effects of loss of reflex co-operation, that attention must be directed for an explanation of the electromyographic changes. If the execution of all normal voluntary movements be regarded as resulting from graded liberation from control of peripheral proprioceptive reflex mechanisms, then it is easy to see how the impairment of these mechanisms may account for such serious disturbances as are found in tabes dorsalis. But the balance of evidence is in favour of direct motor innervation in a positive sense from a higher level, and it seems probable that adjusted movements involving nice degrees of co-ordination between different muscle groups are not carried out by innervation distributing mechanisms in the cord. While it is probable that these innervation patterns have been learnt laboriously under the guiding influences of sensory proprioceptive control, it is difficult to believe that after years of practice they could be so grossly disturbed by a defect on the sensory side alone as may be seen in some cases of tabes dorsalis.

Involuntary movements and spinal reflexes.—v. Weizsacker [76] studied the electromyograms from muscles active during spinal, co-ordinated, reflex responses to cutaneous stimuli. He found that some of these were identical with those of voluntary movements. Others showed single large active currents separated by intervals of quiescence or of short tetani, the duration of individual deflections being increased. From the fact that, in spite of complete functional interruption of the spinal cord, such movements below the level of damage may yield normal "voluntary" electromyograms, he concluded that the form of the deflection curve for voluntary movements must be determined at the level of the anterior horn cells.

Persistent clonus in spastic muscle may be associated with single action currents occurring at the same rate as the contractions (Gregor and Schilder knee-clonus, 7 to 9 per second) or with small groups of action currents. (Gregor and Schilder hand- or ankle-clonus 2 to 4 waves, Bornstein and Sanger [11] ankle-clonus 3 to 5 waves at $\frac{1}{50}$ second intervals). Gregor and Schilder thought that there was probably only one motor discharge per beat, and that interference at the muscle equator of action currents arising in different parts of the muscle lead to its apparent reduplication in some cases. Hoffmann, Hansen and Weizsacker [40] found that each clonic beat from the calf muscles in a case of cerebral diplegia was associated with a volley of several large deflections. They also made the observation that each tendon-jerk obtained from a spastic muscle is followed by a temporary inhibition of the pre-existing spastic discharge.

Involuntary movements—chorea.—Bornstein and Sanger [11] described for chorea an electromyographic picture having "an extraordinary resemblance" to that of paralysis agitans, in that the action currents of increased duration (0·03 second) occurred at a lower frequency (30 per second). From these observations they concluded that the conduction time in the muscle, from the region of nerve-entry to the extremities, was increased. However, records differing in no wise from those of normal voluntary movements have been obtained and described by Gregor and Schilder [31], Salamonson [61] and Cobb [12].

Rehn [57] describes records from a case of torsion dystrophy as being normal in appearance except for a tendency for the occurrence of prolonged groups (lasting $\frac{3}{4}$ to $1\frac{3}{4}$ seconds) of regular action currents at 45 per second.

Although Fröhlich and Meyer had found no action currents associated with maintained cataleptic attitudes when using skin-pad electrodes, Rehn [56] obtained normal electromyograms from the same condition with needle electrodes, a result confirmed by Hoffmann and Weizsacker. Normal records from cases of hysterical movements have been obtained by Rehn [56] and Cobb [12].

Convulsive state and contractures.—That the muscular cramps or spasms associated with some cases of amyotrophic lateral sclerosis give electromyographic records similar to those of normal voluntary movements has been reported by Hoffmann [39], and Hoffmann, Hansen and Weizsacker [40], although Bornstein and Sanger [11] had previously found action currents absent in this condition.

Tetanic spasm has been described as unassociated with any form of action current by Salamonson [61] and Semereau and Weiler [64].

VII.—SUMMARY.

(1) A short account has been given of the previously recorded electromyograms of normal voluntary movements in man. These have been compared in respect of the amplitude, form and frequency of their individual deflections.

(2) An attempt has been made to outline the principles governing the interpretation of such records in terms of muscle activity and expressed in terms of the electrical and mechanical components of such activity.

(3) The principles underlying the known distribution of the electric field about active, simple muscle strips surrounded by a conducting medium have been applied to the case of skeletal muscle voluntarily made active in the intact limb.

(4) The inferences permissible with regard to the motor discharge from the central nervous system during voluntary movements have been stated and the factors governing this discharge examined.

(5) A suggested explanation for the so frequently observed dominant 50-per-second rhythm has been advanced.

(6) The influence of fatigue upon the action currents of voluntary movements has been detailed. The effects of such fatigue have been correlated under the term "effort syndrome" and the other conditions and modes of occurrence of this effort syndrome stated.

(7) An attempt has been made to determine the site of the mechanism responsible for the phenomena of the effort syndrome. As a result of the inquiry the existence of a mechanism having certain properties and located in a certain part of the reflex system has been postulated.

(8) Short summaries have been made of the recorded characteristics of the voluntary electromyograms obtained from patients suffering from different pathological conditions.

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PROGRESSIVE HYPERTROPHIC POLYNEURITIS, WITH CASE REPORTS.

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PROGRESSIVE hypertrophic polyneuritis was first described in 1899 by Goubault and Mallet [6], and four years later was designated as a new clinical entity by Dejerine and Sottas [4], with whose names the condition is usually associated.

Pathological confirmation of the diagnosis in a number of published cases shows that the clinical picture varies within very wide limits, while the pathological changes themselves vary both in detail and in degree. Thus there may be no family history of similar disease, as in cases reported by Boveri [2] and Dide and Courjon [5]; the disease may begin in adult life (De Bruyn and Stern [3], Harris and Newcomb [7], and Long [8]); the course may be characterized by remissions [7]; and the degree of peripheral nerve enlargement may be slight [3, 4, 7], or very great, as in the cases reported by Boveri and Souques and Bertrand [11].

Pupillary abnormalities, nystagmus and kypho-scoliosis, originally described as features of the disease, have been present in a few cases only; exophthalmos in one family [2] and persistent diarrhœa in cases reported by Pierre Marie [9] introduce additional features.

The wide variations in the symptomatology make any attempt at describing types of the disease valueless, and it must be acknowledged that there are only two constant clinical features, namely, muscular atrophy and the peculiar enlargement of the peripheral nerves.

The cases here described illustrate again the variability in the clinical picture. Case 1 shows extreme wasting and enlargement of all the peripheral nerves in a young adult; in Case 2, on the other hand, wasting of one hand was noticed for the first time at the age of 38; pes cavus had been present since childhood, and five relatives show neurological changes probably related to the same condition.

Cases 1 and 2 have been fully examined as in-patients at the National Hospital, and the diagnosis has been confirmed by biopsy. The other five patients have been visited at home, and are not under medical supervision.

Case 1.—G. F., female, aged 32, was admitted to hospital under Dr. Macdonald Critchley on February 7, 1930, complaining of progressive weakness and numbness of the limbs with wasting of the hands and feet.

There was no history of illness in the parents, who had one other child; this child had tuberculous cervical adenitis, but is now a healthy and active man. No history of illness in more distant relations is available.

The patient suffered from measles, whooping-cough and chickenpox as a child, and had a severe attack of influenza in 1918 (when the temperature reached 105° F.). She had been troubled with cough all her life; there had never been sputum or hæmoptysis, but there was an attack of pain in the chest several years ago. For the past few years there had been dyspnœa on exertion and steady loss of weight, though she had never weighed more than 8 st. Menstruation was regular until she was 24, when there was amenorrhœa for four years; the menses were regular from 1926 to 1929, but since then there has been complete suppression.

The first definite symptom of the present illness was weakness of the legs, first noticed five years ago. About a year later weakness of the hands developed. This weakness steadily progressed, and was always more marked in the summer or if she was in a hot room. For several years there had been attacks of stabbing pain all over the body, but most marked in the hands and feet, and worse in the summer months. Numbness of the hands and feet had been progressive throughout, and she stated that she knew nothing of her feet unless she could see them; she was unable to stand on her bare feet. The colour of the feet, and to less extent of the hands, varied from purple to a vivid red, according to the room temperature. She had noticed a flickering sensation under the skin and had seen the flickering from time to time. There had been no sphincter disturbance.

Examination.—The patient is a small, emaciated woman (weight 5 st. 8 lb.). She is intelligent and shows no abnormality of higher cerebral functions. The fundi and pupillary reactions are normal, there is a rapid, ill-sustained nystagmus on looking to the right, and a mild degree of bilateral ptosis. The lower part of the right side of the face is weak both in voluntary and emotional movements. The other cranial nerves show no abnormality. There is generalized wasting of both arms in proportion to the general emaciation, with well-marked distal accentuation which becomes extreme in the intrinsic hand muscles, especially on the thenar side. Grip is moderately good on both sides, but there is extreme weakness of all the intrinsic hand muscles. There is a fine rapid tremor of the outstretched hands as well as a slower, coarser and more irregular movement of the fingers. Both arms are slightly hypotonic; the finger-nose test is accurately carried out.

There is extreme wasting of the legs, which begins at the junction of the middle and lower thirds of the thigh and increases towards the periphery. The feet are inverted and plantar flexed. There is a full range of active and passive movements at the hips and knees, though all movements are weak. There is practically no active movement at the ankle-joints, and passive dorsiflexion is limited and painful. Tone is diminished in both legs. The heel-knee test is carried out on both sides with slight inaccuracy. The trunk muscles are strong and are not wasted. Fibrillation is occasionally seen in the arms and thighs. Gait is steady and progress fairly rapid, but the feet are lifted very high; there is a good deal of unsteadiness when turning and well-marked Rombergism.

There is considerable sensory disturbance. Pain sensibility is practically lost over the arms and fore-arms and between the knees and ankles, though there is little impairment over the hands, feet and trunk. Light touch is everywhere normally appreciated. Temperature sensibility is only lost over the feet. Two-point discrimination is very defective over the hands and feet, and vibration is not appreciated below the knees. The sense of position and of passive movement is very defective in the toes, but is not impaired in the fingers. Deep pressure pain is lost below the knees. There is intense vasomotor change in the feet, with a less marked change and excessive sweating in the hands.

There is a great and generalized enlargement of the peripheral nerves; the nerves are hard and painless and are especially noticeable in the upper arm and neck. The internal cutaneous nerve of the arm is visible as a thick, beaded cord (fig. 1) and there is extreme enlargement of the ulnar and external popliteal nerves.

All the tendon-jerks are very sluggish and the supinator and ankle-jerks are absent. The abdominal and plantar reflexes could not be obtained.

The chest is long and narrow with impaired movement on the right side; the percussion note is impaired at both apices, and there is prolonged expiration with numerous crepitations all over the chest.

The nails are lilac tinted.

X-rays show opacity at the right apex with numerous areas of infiltration throughout both lungs.

Special investigation.—Blood-pressure is 130/84 mm. The red-cell sedimentation 7·5 in one hour. The blood-Wassermann reaction is negative. The resting blood-sugar is 100 mgm. per cent. with normal curve after the ingestion of glucose. There was no sputum and no tubercle bacilli in the fæces. "All the muscles of the arms, fore-arms and hands show partial reaction of degeneration; the faradic response can be obtained with large currents; the galvanic response is typically sluggish. The muscles of the thigh also show partial R.D. The muscles of the legs show complete R.D., no faradic response being obtained with bearable currents" (Dr. L. W. Bailey).

On admission to hospital the evening temperature was 99° F. and the pulse-rate 100. Following the administration of potassium iodide, the temperature rose to 101° F. and the pulse-rate to 120.; cough increased but remained unproductive. On withdrawing the iodide the temperature and pulse-rate fell to their previous levels.

Appetite improved on giving insulin (5 units t.d.s.), but weight remained stationary.

A biopsy was performed under local anæsthesia and a piece resected from the internal cutaneous nerve of the left arm. This was irregularly thickened, varying from 5 mm. to 3 mm. in diameter (fig. 2). On cross-section about three strands of homogeneous gelatinous tissue were seen; the finely fibrillar structure of the normal nerve was completely lost.

Celloidin sections stained with van Gieson showed each of the three strands to be surrounded by a definite, and probably normal, perineural sheath; and in this lay sparse nerve-fibres considerably separated from one another, each being surrounded by a thick zone of concentrically arranged connective tissue fibres derived from the endoneurium. Few nuclei were seen in these zones, but there were usually one or more nuclei near the centre in which was a clear ring representing the myelin sheath and axis-cylinder. A few nuclei and scattered strands of collagen running longitudinally were seen in the tissue separating the nerve-fibres, the rest of which appeared structureless and took on a faint yellow colour with this stain. When stained by the Weigert-Pal method, most of the nerve-fibres showed a definite, though thin, myelin sheath, and in longitudinal section this was seen to run uninterrupted when present (fig. 3). Occasionally two myelinated fibres were seen to run in one endoneural sheath. In the interstitial spaces were seen large irregular cells with clear cytoplasm and large irregular nuclei; these appeared to be of endothelial origin.

Case 2.—W. I., male, aged 38, was admitted to hospital on March 24, 1930, under Dr. Kinnier Wilson, complaining of wasting of the right hand.

He was quite healthy as a small boy and was able to play football and other games. After he left school (aged 14) his toes began "to contract" and his feet to change shape. He then found that he could not run so well as formerly and that he was less steady on his feet. This disability in his feet has not progressed during the last twenty years.

He drinks about one glass of beer per week. He is a storekeeper and frequently handles lead while at work.

Three and a half months ago, coincident with the onset of colder weather, he noticed some numbness of the index finger of the right hand, and that when his hands were cold his pen used to slip out of position. There was also some wasting of the hand about which he consulted his doctor. No symptoms suggestive of plumbism were present. He remains quite fit for his work and spends all day on his feet. There have been no other symptoms.

Examination.—The patient is a healthy looking man of spare physique and average intelligence. There is no abnormality of speech or of the higher cerebral functions. The fundi and pupillary reactions are normal. The external ocular movements are full and there is no ptosis or strabismus. Fine horizontal nystagmus is present on looking both to the right and to the left, the quick component being in the direction of gaze. (This is not constantly present.) The other cranial nerves show no abnormality.

There is considerable wasting of all the small muscles of the hands and of the fore-arms, especially in their distal halves. This is much more pronounced on the right side. Power is diminished in proportion to the degree of wasting. There is no weakness or wasting of the upper arms.

The outstretched arms maintain their posture, but small movements of the fingers are seen on both sides and are associated with fibrillary twitching in the muscles. Co-ordination tests are accurately performed. No abnormality of muscle tone was detected. There is marked upper dorsal scoliosis, convex to the right. The trunk and abdominal muscles show no abnormality.

There is bilateral pes cavus. Wasting of the anterior tibial and peroneal muscles is marked in both legs, and this is associated with marked weakness. There is no weakness of movement at the hip or knee on either side. Co-ordination is good. No fibrillation is seen in the lower extremities.

"All the intrinsic muscles of both hands show partial R.D. as well as the flexors of the right fore-arm. The extensors of the right fore-arm gave normal responses. In the right leg the tibialis anticus, peronei and extensor digitorum brevis show complete, and other muscles partial, R.D. All muscles of the left leg show partial R.D." (Dr. L. W. Bailey.)

All the tendon-jerks are absent. The abdominal reflexes are present, but sluggish. Both plantar reflexes show frank extensor responses (no weakness of the toe flexors).

There is no sensory loss to pin-prick or cotton-wool. Temperature sensibility, sense of position and passive movement are all normal and vibration is normally appreciated. There is no tenderness of the muscles, but the soles of the feet are unusually sensitive.

There is considerable enlargement of all the peripheral nerves. The median nerves in the cubital fossæ are particularly large, and the course of some of the cutaneous nerves of the fore-arm is visible through the skin. The nerves are firm and their surface feels slightly irregular. They are not tender on firm pressure.

The gait is steady and brisk. There is a drop-foot on the right side. Romberg's sign is not present.

Examination of the cardiovascular, respiratory and genito-urinary systems reveals no abnormality.

Special investigation,—The cerebrospinal fluid is clear and colourless, cells 4 per c.mm. (20 per cent. large mononuclears), total protein 0·10 per cent., Nonne-Apelt test weakly positive, Pandy test negative, Lange 0011100000, Wassermann reaction negative. Blood Wassermann reaction negative. X-rays show absence of cervical ribs; a fractional test meal shows complete achlorhydria (total chlorides 0·3 per cent. after one hour). The blood-picture is normal.

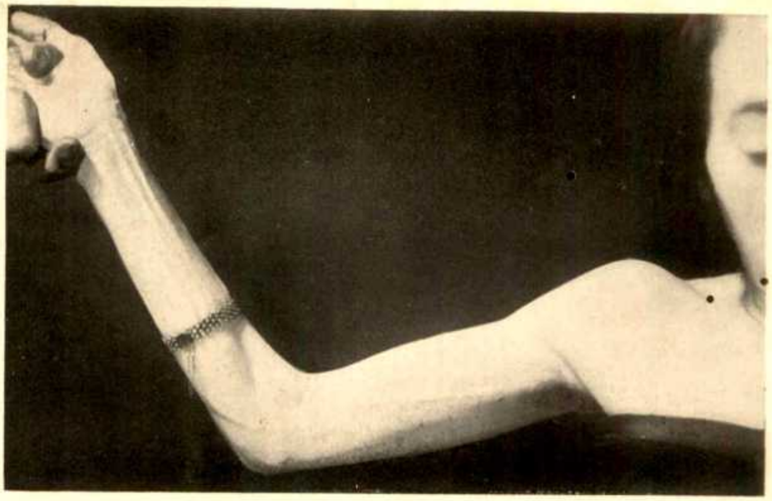


FIG. 1 (*Case* 1).—Showing the nodular enlargement of the internal cutaneous nerve.

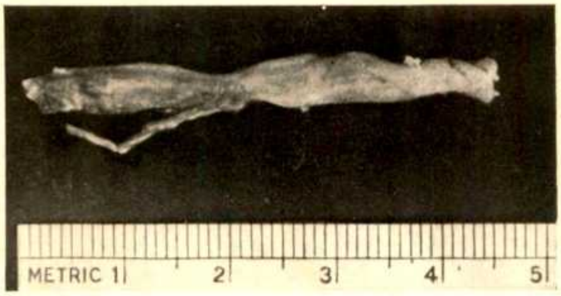


FIG. 2 (*Case* 1).—Resected portion of internal cutaneous nerve.

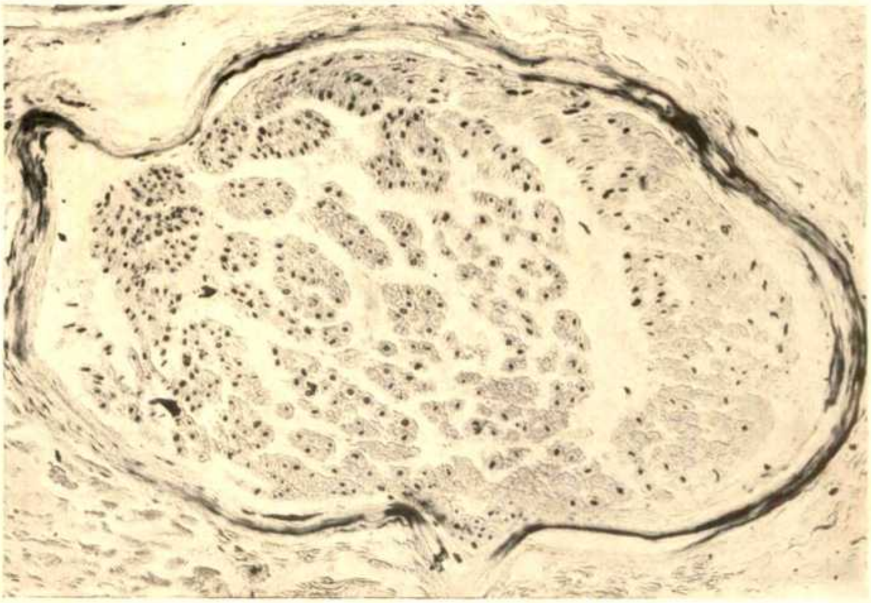


FIG. 3 (*Case* 1).—Cross section of nerve. Weigert-Pal stain.

To illustrate paper by W. Ritchie Russell and Hugh G. Garland.

PLATE XVIII.

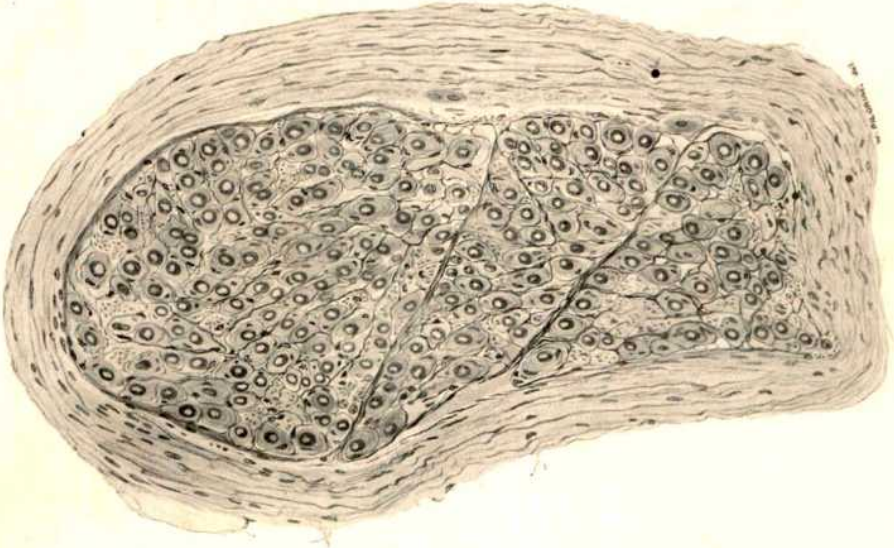


FIG. 4 (*Case* 2).—Cross-section of a bundle in the nerve resected. To show the thickening of the endo- and peri-neurium. Scharlach R. × 200.

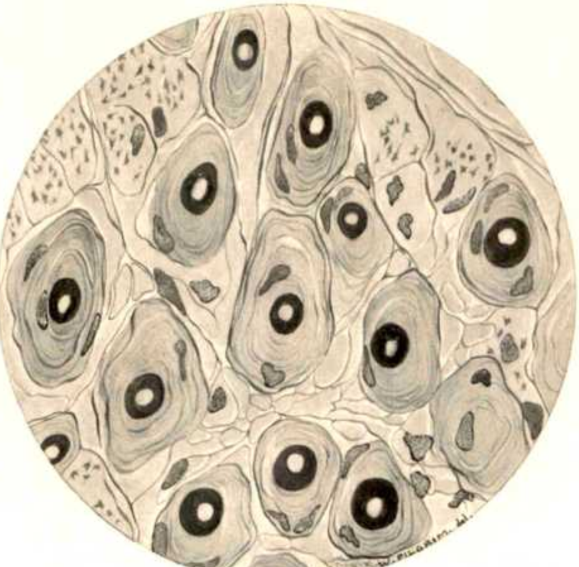


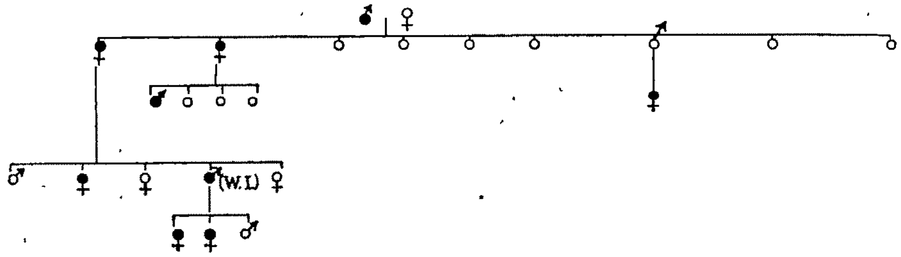
FIG. 5 (*Case* 2).—A portion of the same bundle under a higher magnification to show the nuclei and concentric lamellæ in the endo-neurium. Scharlach R. × 1,000.

To illustrate paper by W. Ritchie Russell and Hugh G. Garland.

A portion of the internal cutaneous nerve of the left arm was removed under local anæsthesia.

Frozen sections show some separation of the individual nerve-fibres by fluid or mucoid infiltration. Each individual myelinated fibre is also surrounded by several concentric layers of connective tissue capsule which form a zone at least as wide as the transverse diameter of the myelin sheath. In celloidin sections, in which the nerve-fibres are more shrunken together than in frozen sections, the appearance is that of isolated myelinated fibres separated from one another by dense and fairly wide envelopes of fibrous tissue (endoneurium). The perineurium is much thicker than normal. The interstitial spaces appear to contain more nuclei than are seen in Case 1, in which the condition is more advanced (figs. 4 and 5).

Family history.—A history of some abnormality apparently related to this patient's condition was found in eight other members of his family. Five of these have been examined (fig. 6).



● = shews neurological abnormality (described in text).
o = apparently normal

FIG. 6.

The patient's mother's father died of a stroke at the age of 65. He had curvature of the spine and used to lift his feet high when walking. His feet were very small, but no deformity was noticed. Patient's mother had nine brothers and sisters, none of whom was in any way abnormal.

Case 3.—The mother of Case 2 is now aged 65; she has had difficulty in walking ever since she had a severe attack of rheumatic fever when aged 15. She has had to wear special boots since that time owing to deformity of the feet. She has suffered severely with "arthritis" for twenty years, which has necessitated her using a bath chair. She has had stabbing pains in the hands for twenty years.

Examination.—The pupils react sluggishly to light. The outstretched hands are tremulous. All the tendon-jerks are absent, and the plantar reflexes are indefinite. There is very pronounced pes equino-varus on both sides, and gross arthropathy with disorganization of both knee-joints, allowing about 40°

of lateral movement, and extreme genu valgum on attempting to stand. Passive movement of these joints causes little pain and they resemble very closely the Charcot's joints of tabes dorsalis. There is considerable arthritis of the joints of the fingers, causing awkwardness and weakness of fine movements of the fingers. No fibrillation was seen. No sensory loss to pin-prick, nor to light touch, nor loss of appreciation of passive movements was detected.

This patient has five children alive —

Al., male, who is quite normal.
Al., female, aged 42, affected (Case 4).
E., female, aged 40, quite normal (with children).
W., male, aged 38, affected (Case 2).
Et., female, aged 34, quite normal (with children).

Case 4.—Al., female, aged 42, has had difficulty in walking since the age of 12, together with deformity of the feet. There has been wasting of the right hand for the past seven years. Four years ago she had severe pains in both hands and fore-arms for seven weeks, and following this great weakness of the hands developed. This has improved considerably since then. Five years ago there was some numbness in her right hand.

Examination.—The pupils are of average size, but react sluggishly to light. There is ill-sustained nystagmus on lateral deviation of the eyes. The cranial nerves show no other abnormality. There is pronounced wasting of all the small muscles of the hands, especially of the first dorsal interossei; the right hand is more affected than the left. There is also wasting of the distal half of each fore-arm.

There is a marked degree of bilateral pes cavus and there is some wasting of the muscles below the knees. The feet are very cold. All the tendon-jerks are absent. The plantar responses are both flexor.

There is some diminution to pain sensibility over the right foot, and the lower part of the leg, but there is no other sensory loss. The accessible nerves are easily palpable and are probably larger than normal; they are hard and not at all tender on deep pressure.

Case 2 has three children :—

J. I., female, aged 13 (Case 5).
C. I., female, aged 11 (Case 6).
A. I., male, aged 7, who was examined and appeared to be quite normal.

Case 5.—J. I., female, aged 13, is quite healthy, but her hands have always been shaky, especially in the morning. She is apt to fall while playing games. An operation for bilateral pes cavus was performed at the age of 11½ years.

Examination.—She is well-developed physically and mentally. There is some ill-sustained nystagmus on looking to each side. The outstretched hands are tremulous and are a little unsteady in co-ordination tests

All the tendon-jerks are absent; the plantar responses are flexor. No sensory loss was discovered.

The accessible nerves are easily palpable; they are hard and are not tender on deep pressure; they are probably not enlarged.

Case 6.—C. I., female, aged 11, has always enjoyed good health. She had "St. Vitus' dance" at the age of 2, but has had no other illnesses. The mother thinks she is normal in every way.

Examination.—She is a well-developed child, both physically and mentally. The pupils are normal. There is ill-sustained nystagmus on looking both to the right and left. No tremor or other motor disturbance was observed.

All the tendon-jerks are absent; the plantar responses are both flexor. There is no deformity of the feet and no sensory loss could be detected.

Case 7.—B. W., female, is a first cousin of W. I. (Case 2), being the daughter of his mother's brother. She has no brothers or sisters; her mother has had no miscarriages. The patient became unsteady on her feet at the age of 7, and has become steadily worse. She has developed curvature of the spine. An operation was performed on both feet when she was 14, but there was no improvement. A year ago she had an acute febrile illness with swelling of both knees, and on recovering from this she noticed numbness and "pins and needles" in both hands, and experienced some difficulty in using them. This disability has improved since then. She has no pain now except in her feet.

Examination.—The patient is thin and pale; she is normally developed mentally. The pupils are normal. There is ill-sustained nystagmus on looking to the right and to the left. The other cranial nerves show no abnormality. There is no obvious wasting in the upper limbs, but there is some tremor of the outstretched hands, especially the right. Power in all muscle-groups is fair. She can hyper-extend her fingers at the metacarpo-phalangeal joints to a right angle. She has marked kypho-scoliosis and an extreme degree of club-foot on both sides. The range of movement at the ankle-joints is very small, the dorsiflexors of the feet being especially weak. There is no gross wasting of the legs.

All the tendon-jerks are absent; the plantar reflexes are doubtful. No sensory loss to pin-prick was discovered; sense of position is normal. Light tactile stimuli are not normally appreciated over irregular areas of her legs.

All the palpable nerves are enlarged; they are hard, and are not tender on deep pressure.

This patient's mother's sister has four children; none of these was examined, but one, aged 36, "has something wrong with his feet."

DISCUSSION.

Various opinions have been expressed with regard to the nature of this disease and its relationship to other familial conditions.

Marinesco, Raymond, Bedaschi and Long [8] have regarded it as a variety of Charcot-Marie-Tooth's disease. On the other hand, Souques

[10] and de Bruyn and Stern [3] have claimed a separate identity for hypertrophic neuritis, both clinical and pathological.

The close resemblance to peroneal atrophy is shown by Case 1, but there was also the rosary-like enlargement of the nerves which Bielschowsky [1] considered to be one of the features which related these cases to von Recklinghausen's neuro-fibromatosis. Enlargement of the peripheral nerves is a well-known phenomenon in von Recklinghausen's disease and has been described by Thomson [12] in his monograph on this subject.

The presence of a definite extensor plantar response in Case 2, and of a doubtful response in Cases 3 and 7, suggests a possible relationship between hypertrophic neuritis and the familial ataxias.

Despite the close relationship to other diseases which is sometimes apparent, it seems advisable to regard the condition as a separate entity until more conclusive evidence of its relationship to other diseases is established.

SUMMARY.

(1) Progressive hypertrophic polyneuritis appears to be a clinical and pathological entity.

(2) The symptomatology is extremely variable. Enlargement of the nerves and wasting of muscles are the only constant changes.

(3) Seven cases are described, in two of which the diagnosis has been confirmed by microscopic examination of the nerves.

(4) In this series nystagmus and absence of tendon-jerks are common to all the cases.

We wish to thank Dr. Kinnier Wilson and Dr. Macdonald Critchley for permission to publish these cases, and to express our indebtedness to Dr. J. G. Greenfield, who has directed the pathological investigations and kindly supplied the photomicrographs.

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NOTICES OF RECENT PUBLICATIONS.

Les Plexus Choroïdes. Par Dr. NATHALIE ZAND. Pp. 140. Paris: Masson et Cie. 1930. Price 44 francs.

This essay on the choroid plexus is divided into three chapters which deal respectively with the anatomy, physiology and pathology of the plexus and the structures with which it is in intimate relationship, especially the cerebrospinal fluid and the ependyma.

The chapter on anatomy is concise and straightforward enough, but in attempting to deal with the physiology of the choroid plexus and cerebrospinal fluid, the author has become involved in a maze of conflicting and even contradictory theories and observations from which she makes but a half-hearted attempt to extricate herself. Much of this confusion might have been avoided if she had paid as much attention to the latest work as she has to some older observations. The chief criticism which will be levelled against this part of the book is that it completely neglects the Donnan membrane theory in its relation to cerebrospinal fluid circulation, on which so much recent work is based. In the chapter on pathology some useful facts are collected, but the limited nature of the author's material has prevented her from adding much of importance. She is satisfied, however, that there is little qualitative difference in the effect which different diseases and intoxications produce on the choroid plexus. The chief differences lie in the fact that acute conditions affect the epithelium and more chronic ones the vasculo-conjunctival structure of the plexus. This chapter contains some material which is unfamiliar to most neurologists, and is of more value than the rest of the book.

Teknik der Microskopischen Untersuchung des Nervensystems. von W. SPIELMEYER. 4th Auflage. Pp. 168. Berlin: Julius Springer. 1930. R.M. 11.40.

The fourth edition of this valuable laboratory handbook preserves the format of the last edition, and is little increased in size, in spite of the addition of much new material. This has been made possible by the sacrifice of older methods as they are replaced by newer ones. For example, old-established methods for staining neuroglia, such as those of Bevan Lewis and of Bethe, have been omitted to make room for the various modifications of Hortega's silver methods. We are glad to see the inclusion of several English methods which were absent from the last edition, such as Anderson's Victoria blue stain for neuroglia, Perdrau's silver stain for fibroglia and Laidlaw's method for peripheral nerve-fibres. Another welcome addition is the enlargement of the section on the staining of spirochætes in nervous tissue.

In a book of this size it is impossible to include everything, and two notable omissions are Busch's osmic acid method for myelin degeneration, and the use of formol saline or of Kaiserling's fluid as fixatives. It is indeed surprising to see that a solution of formalin in water is still recommended as a fixative for the nervous system. But every laboratory worker has his individual preferences, and it appears to be impossible, especially with the nervous system, to standardize technique. It is therefore all the more valuable to have a description, in a compact and practical form such as this, of the technique used in the Kaiser Wilhelm Institut at Munich.

Nouveau Traité de Psychologie. Par GEORGES DUMAS. Tome I. Notions préliminaires. Introduction. Méthodologie. Pp. 425. Paris: Alcan. 1930. Price 75 francs.

This is the first volume of a series in which normal psychology (in eight volumes) and pathological psychology (in two) are to be presented by such noted French authorities as Janet, Claparède, de Clerambault, Séglas, Piaget, Pieron, Levy-Bruhl and many more.

The present volume is mainly introductory. Articles on the place of man in the animal series and on the data of anthropology are tokens of thoroughness in the general plan of the work—the first by Perrier, the second by Rivet. The physiology of age and sex is dealt with by Champy, Pézard's work in this field naturally receiving much attention; conformably to the present state of knowledge the writer confines himself largely to comparative observations, with none of those hardy incursions into conjecture and ill-founded affirmation which are met with, especially among psychiatrists, in this matter. Lapicque, known for his distinguished research into chronaxy, deals with the general physiology of the nervous system, chiefly in the light of his special studies. Tournay's competent article on the special physiology of the nervous system is followed by a chapter of great interest by Henri Wallon on the biological problems of consciousness; the influence of von Monakow is here strongly in evidence, and the "phenomenology" of Jaspers is discussed in some detail. At this point the "notions préliminaires" come to an end, and there follow the first two chapters of Book I—an introduction to psychology by G. Dumas, the general editor of the series, and André Lalande's conspectus of methods and aims in psychological investigation.

In this volume the discussion ranges, as one would expect, from philosophy to physiology, but it is balanced and restrained. The bibliographical lists are by no means restricted to French works. The volume is well illustrated, but has no index.

The Psychology of Insanity. By BERNARD HART. Pp. 176. Cambridge University Press. 1930. Price 3s.

Dr. Hart's well-known little book appears in the fourth edition, little changed from its first form of eighteen years ago. An introduction has been added dealing chiefly with the development of psychopathology as expressed in the teaching of Janet and Freud, and most of the footnotes of former editions have been taken up into the text. It is scarcely necessary to say that the book fulfils its modest aims admirably; intended for the beginner and the layman, its simplicity is a merit, even though it fails to indicate the great complexity of the problems concerned.

The Basis of Epilepsy. By EDWARD A. TRACY, M.D.(Harvard), Director of the Epileptic Clinic at Forsyth Dental Infirmary, Boston. 1930. Rich. G. Badger, Boston, U.S.A. Pp. 88.

The thesis of this work is based upon the observation of the intense colour and duration of the white streak of vaso-constriction that followed stroking of the skin in epileptics with grand and petit mal. The time variability in addition to the above were noticeably different from that in normal control cases.

The book contains the time observations in detail of the whole investigation, and is illustrated with pictures of the reaction, and of the methods for eliciting it. The author argues from these findings to the conclusion that epilepsy must be regarded as a clinical entity having vaso-motor capillary constriction in the brain as the physio-pathology of the disorder.

Medizinische Psychologie. von ERNST KRETSCHMER, Professor für Psychiatrie in Marburg. 1930. Leipzig: Geo. Thieme Verlag. Pp. 259. Price 16 marks.

This is the fourth and enlarged edition of this now celebrated volume. The book is written in the light of fundamental principles. The well-known reaction type theory of its author is fully discussed, and his biological theory of hysteria is also given in extended form. This book only awaits translation to make it more widely and deservedly accessible to all English psychiatrists.

The Mental Development of the Child, By KARL BÜHLER, Professor in the University of Vienna. 1930. London: Kegan Paul. Pp. 170. Price 8s. 6d.

The author has brought together in a brief space the contents of a larger work on the psychology of the child. It attempts to trace the biological foundations of child psychology, and in consequence passes systematically through child development, pausing to consider inheritance of mental qualities, and dealing at length with the perceptual world of the child. Imagination is considered in general, and in particular by reference to its operation in fairy tales. A particularly good chapter is devoted to the development of drawing. The shortcomings of the book are obvious in the treatment of the affective life and the inner life of fancy. The contact with other human beings, particularly the parents, who have the first and lasting influence on the instinct and emotional life both in increasing and in deflecting affectivity, is not dealt with at all. It is now generally admitted that some of the striking features of child life spring from these affective relations to the parents. The author apparently has no use whatever for this approach, and entirely ignores the work of Freud.

Eidetic Imagery, and Typological Methods of Investigation. By E. R. JAENSCH, Professor of Psychology in the University of Marburg. 1930. London: Kegan Paul, Library of Psychology. Pp. 136. Price 7s. 6d.

The classification of human beings according to their imagery exercised the mind of Francis Galton. Little did he appreciate, however, the extent to which the study of imagery under laboratory conditions could be applied to the wider fields of medicine and psychology. In this work Professor Jaensch, who has with his brother been a pioneer of experimental work on a type of imagery, the eidetic, has outlined the method of detecting this type of imagery. The eidetic image differs from both after images and memory images in that it is more closely related in form and behaviour to actual perception. This typological study is no mere exercise in academic psychology, for it digs deeply into the psycho-physics of the human organism. For example, it is found that there is a variability of the eidetic image in relation to calcium metabolism. So much is this the case that the author has discovered a relationship between this type of imagery and tetanoid and basedowian syndromes. The image variations thus studied are not to be regarded as pathological, but are due to functional peculiarities of the autonomic system characteristic of certain youthful stages of development.

Linked with the Jungian classification of mental types, and with Kretschmer's type classification, the application of Jaensch's work to both pedagogics and psycho-pathology promises much fruitful discovery.

The Laws of Feeling. By F. PAULHAN. 1930. London: Kegan Paul. Pp. 208. Price 10s. 6d.

This carefully reasoned essay was not sufficiently known in England, and there is now no excuse for English readers to ignore a theory of feeling which must have a profound effect on the theories of emotion. Hitherto English psychology has been held by the theory of MacDougall. The thesis is, broadly, that feelings as well as emotions are not the accompaniments and tone colourings of the instincts in action, but are due to arrested tendency. It rests still more profoundly on the author's view that man is essentially an unadapted animal, and that feeling and emotion are the results of this maladaptation.

Psycho-pathology, from much of its data relative to repression and the symptom complexes that spring from it, lends support to this theory; and neurology, too, particularly the relationship of autonomic function to the thalamus, gives facts corroborative of this theory.

This is a book that no thoughtful-minded psychiatrist can afford to ignore.

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of "Brain." If reprints are required in pamphlet form, with wrapper, title-page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BALE, SONS & DANIELSSON, Ltd., 83-91, Great Titchfield Street, London, W.

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To those who are not members of the Neurological Section of the Royal Society of Medicine the price is 8s. 6d. net, and the volume may be obtained through any bookseller.

EDITOR.

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DISSEMINATED SCLEROSIS IN NORTH WALES.

AN INQUIRY INTO ITS INCIDENCE, FREQUENCY, DISTRIBUTION AND OTHER ÆTIOLOGICAL FACTORS.

[This work was done with the aid of a grant from the Medical Research Council.]

BY R. S. ALLISON, M.D., M.R.C.P.

I.—INTRODUCTION.

THE first to describe a case of disseminated sclerosis in this country was Moxon. To-day, though much is known of the symptoms, histology and morbid anatomy of the disease, the ætiology and pathogenesis are still obscure. In the latter half of the nineteenth and early part of the present century, histories of cases were collected and analysed and such factors as shock, injury, infectious diseases and intoxications related to the onset of symptoms. Since the war, interest in this subject has been revived, probably stimulated by the experiments with animals and attempts to pass on the disease begun by Bulloch in 1913. Papers have been published at home and abroad which suggest that disseminated sclerosis has a selective geographic incidence; that it occurs with greatest frequency in country districts, and in the occupations of farming and wood-working. It should be noted, however, that these conclusions are based, for the most part, on statistical evidence. There is, perhaps, a danger that they may be too readily accepted and influence opinion without first being submitted to closer scrutiny. Indeed, many of the authors concerned, notably Adams, McAlpine, Steiner and Dana, have suggested that it would be advisable to survey given areas or districts for cases of disseminated sclerosis. In this way the mode of living and habits of individual patients could be studied, and the results compared with those of statistical methods on a larger scale. It is possible, too, that by these means a common factor might be discovered which would throw some light on the vexed problem of ætiology.

Though the subject has been approached since then, so far as the writer is aware no work has actually been done on these lines. The idea is attractive, but it is clear that it can only be applied on a small scale in the first instance, if a personal investigation is made of each case. Later, if thought desirable, more extensive surveys could be arranged by a group of workers acting over a larger field. For the single worker the area selected should be small and well defined. In forming conclusions, prevailing local conditions are apt to be a source of error in a small district. This can, however, be avoided by contrasting the living conditions of affected cases with those of the rest of the inhabitants.

With these objects in view, this work was begun in the autumn of 1928. The district selected was North Wales, where the writer was living. This seemed a suitable area to explore. It is well defined and many of the inhabitants live in small secluded towns or isolated farmhouses, the conditions of life offering much variety and scope for comparison. The expenses incurred were covered by a grant from the Medical Research Council, to whom the project was referred in the first instance

II —Description of the Area surveyed.

(*a*) *Size, divisions, geographic features.*—The province of North Wales consists of the counties of Denbigh, Flint, Caernarvon, Anglesey and Merioneth. The total area is approximately 2,430 square miles, and the relative sizes of the various counties may be judged from the accompanying Map (fig. 1).

Anglesey is an island having an undulating surface close to sea level. The land is rocky and marshy in places and for the most part given over to agriculture. Lead and copper deposits are worked at Amlwch. The climate is humid but mild.

Flint is composed of a plateau rising about 500 to 800 ft. above sea level, and is dry and fertile for agriculture and rich in mineral deposits (coal and lead). Low-lying districts are situated at the mouth of the River Clwyd and along the shores of the Dee estuary (Prestatyn, Flint).

Denbigh has an irregular surface, consisting in parts of bleak hills and moorland with small lakes. The fertile Vale of Clwyd however is rich in pasture land. The climate here is mild and comparatively dry. Indeed Rhyl is said to hold the record among seaside resorts in England and Wales for sunshine. The industrial area round Wrexham is rich in minerals. The county is on the whole well wooded and possesses a fair amount of arable land, whilst on the upland farms sheep are reared.

Caernarvon and Merioneth may be considered together as their central portions are occupied by a solid block of mountain ranges separated by deep and secluded valleys. There are numerous lakes, the largest being Bala Lake in Merioneth, about four miles long. Arable land is confined to the valleys, coastal areas and Nevin Peninsula, and

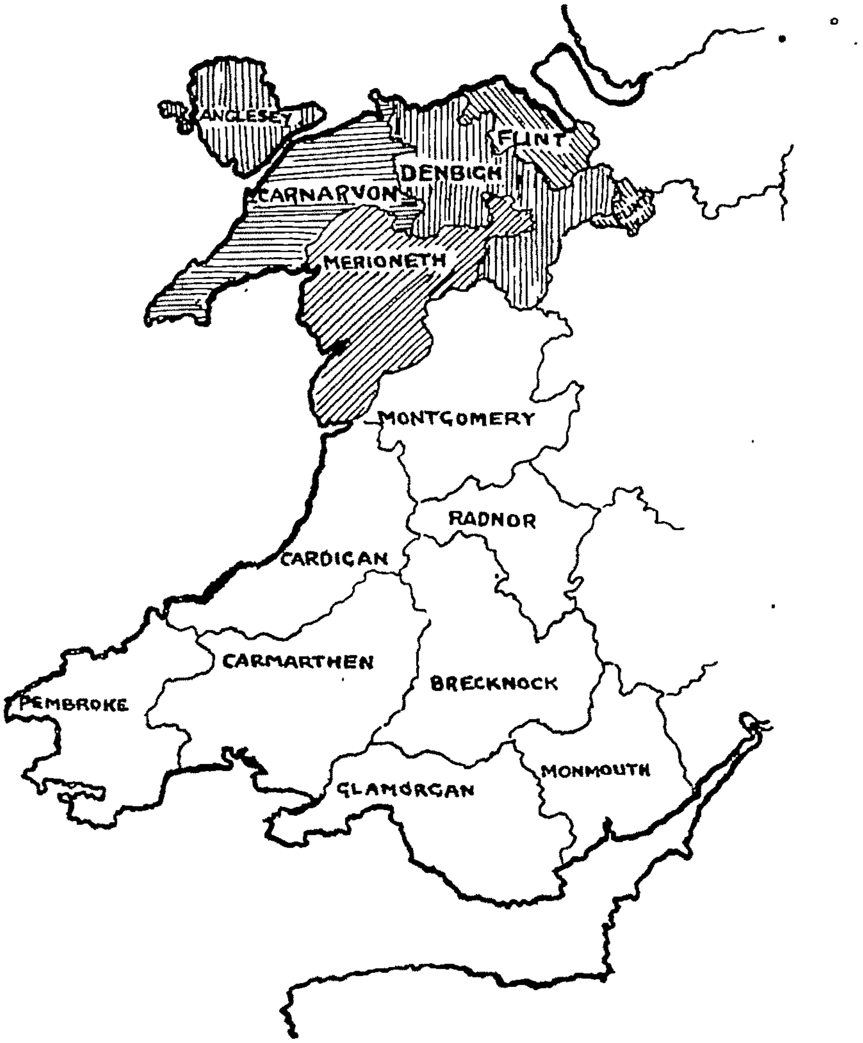

FIG. 1.

sheep and cattle raising occupy the attention of most farmers. The climate is damp and cold in winter.

(*b*) *Population, occupation, rural and urban distribution.*—At the 1921 census the population of the five counties was 489,270 inhabitants, distributed as follows :[1]—

County		Urban districts		Rural districts		Total
Denbigh	..	56,002	..	98,845	..	154,847
Caernarvon	..	68,281	..	62,694	..	130,975
Flint	..	43,224	..	63,393	..	106,617
Anglesey	..	19,789	..	31,955	..	51,744
Merioneth	..	20,255	..	24,832	..	45,087
		207,551 (42 per cent.)		281,719 (58 per cent)		489,270

It is interesting to note that only 58 per cent. of the total inhabitants live in rural districts and 42 per cent. in urban. A higher proportion of rural dwellers would have been expected in such an essentially country district. This is accounted for, however, by the geographic features of Caernarvon and Merioneth. Here, the inhabitants are grouped together in small towns, large tracts of moorland and mountainous country being practically uninhabited. The other counties, and particularly Anglesey, show a strong proportion of rural dwellers as might be expected from their natural features.

There are no cities or large towns, the largest town being Colwyn Bay with 21,566 inhabitants. Other towns of smaller size are Llandudno, Wrexham, Rhyl, Bangor, Holyhead, Blaenau Festiniog and Caernarvon (8,340).

The chief occupation of the province is farming and in the mountainous districts slate quarrying is followed on a large scale particularly in the towns of Blaenau Festiniog and Bethesda. In parts of Flint and Denbigh there are coal mines ; brick, iron and chemical works notably in Wrexham, Buckley, Mold, Hawarden, Flint. Except for these there are no other important industries. Along the coast there are many summer resorts and schools. In these, a number of the inhabitants follow occupations connected with the summer influx of visitors and teaching.

III.—THE METHODS EMPLOYED.

(*a*) *Collection of cases.*—The cases were collected through the courtesy of the medical men in practice in North Wales, to whom the writer is deeply indebted for their friendly and sympathetic help. It was felt that patients could scarcely pass through all phases of the disease without seeking medical advice and the local doctor was the most likely to be first consulted. Disseminated sclerosis is a rare disease in general medical practice. If not recognized as such, the serious nature of the symptoms would prompt the doctor to seek help at the nearest hospital centre. In this way, the cases in his district, if any, would be known to him.

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[1] Information obtained from the County Educational Authorities and Annual Reports of County M.O.H.'s.

From the current medical directory a list of doctors practising in North Wales was drawn up. A letter was then sent to each doctor with stamped envelope and form suitable for reply. The letter briefly set out the object aimed at and asked for information of cases. It was requested that not only should typical established cases be reported but also doubtful or early cases showing one or more of the signs and symptoms associated with the disease. An address was given on the objects of the work at a meeting of the North Wales Branch of the British Medical Association in May, 1929. There was a large attendance and much enthusiasm was raised.

Success, of course, depended entirely on the willingness with which the doctors in practice would co-operate with the objects of the inquiry. Considerable doubt was felt at first on this score, but the results obtained proved this doubt to be entirely unworthy. By the autumn of 1929 replies had been received from practically all the doctors (266 out of 273). This was a sufficient testimony to the willingness of practitioners to help with the research and to indicate that more information relating to the incidence of disease in general might usefully be obtained in this way.

(*b*) *Collection of information relating to cases.*—After notification a suitable day and time were arranged with the doctor concerned and the case visited in his company. Patients were seen at their homes. If the disease had begun elsewhere, so far as possible this place was also visited. Ample time was given to each case to obtain a careful history, make an examination and inspect the living conditions. It was seldom possible to investigate more than one case at a time. As a rule the doctor and responsible relatives were present at the interview. Statements made by the patient could thus be confirmed and supplemented. Without exception, the patients and their relatives gave every help and welcomed rather than discouraged the inquiry.

Altogether 126 cases were reported, 65 of these being cases of disseminated sclerosis. Six of these had been treated in Ruthin Castle during the past five years. The remaining 61 were doubtful cases, or examples of other diseases of the nervous system, such as encephalitis lethargica, neurosyphilis, &c. As a rule the replies from doctors stated that they had no cases in their practice, or that they had one typical case and two or three doubtful ones, presenting one or more of the signs of disseminated sclerosis. It often happened too that when a visit was paid to a district, the writer was asked to see other cases of nervous disease. These doubtful and extra cases were purposely included in the total so that they should serve as controls to the true cases when required. In this way the large number of extra cases reported is accounted for.

The 126 cases were classified as follows:—

Class A.—Typical cases of disseminated sclerosis .. .. = 39
,, *B* —Early cases in which disseminated sclerosis was a probable diagnosis = 10
,, *C.*—Histories of cases deceased or untraceable .. .. .. = 16
,, *D.*—Doubtful cases, symptoms and signs inconclusive .. .. .. = 9
,, *E.*—Examples of other diseases of nervous system .. .. .. = 52

126

With one or two exceptions and excluding Class *C*, the above cases were investigated personally by the writer.

History-taking and examination.—The same routine procedure was followed in all cases. The plan was as follows:—

(1) *Family history.*—Cause of death or state of health of parents and brothers and sisters. Place in the family. Direct inquiry for paralysis, fits, insanity, nervous breakdowns, in other members of the family.

(2) *Injury, shock, exposure.*—Date and relation to onset and course of symptoms. Character.

(3) *Occupation.*—Nature and conditions under which work was done. If more than one occupation had been followed, dates of change noted. Spare time pursuits and hobbies. Leading questions regarding work with wood, animals, agriculture.

(4) *Pregnancy, menses, marriage.*—Age of onset and character of menstruation; menopause. Civil state at onset disease. Effect of confinements on onset and course.

(5) *History of life.*—Place of birth, occupation of parents and early living conditions. Dwelling places in town or country. Accommodation, water supply, sanitation, geographic features. Living conditions at onset of disease inspected for above points. Leading questions, *re* premises infested with rats, damp and cold, contact with animals, farm work, insect bites.

(6) *History of illness.*—Date and character of onset. Remissions and exacerbations. March of symptoms.

(7) *Examination.*—Build and stature. Fair or dark type. Mentality, cranial nerves, motor and sensory functions, reflexes, state of spine and joints. Result of blood Wassermann and examination of cerebro-spinal fluid.

In some the information available was scanty and unreliable, but in many others every facility was afforded for an accurate survey of the habits and living conditions. Much of the data sought was probably irrelevant but it was felt that the inquiry should be as full as possible as a unique opportunity was offered of seeing these patients in their own environment. It is usually difficult to obtain accurate information about family history and previous illnesses from the hospital patient. The patient may be willing enough but his memory will not serve. In this inquiry the help of the family doctor and relatives of the patient was invaluable, and much which otherwise would have been lost is recorded.

The onset of the disease in each case was fixed as accurately as possible. This is a difficult task, especially in cases of long standing. Usually it could be traced back before the date given by the patient. This uncertainty about the onset is admittedly a weak point in relating conditions of life to it. If the habits or circumstances of a person render him liable to develop disseminated sclerosis, it is important that we should be able to fix the date of onset fairly closely. It was a fortunate thing therefore that a number of the patients had lived in the same place and under the same conditions for some years before and after the earliest symptom.

Diagnosis presented difficulty in many cases. So far as possible doubtful cases were excluded and only those with typical features were put in Class *A*. A big proportion had been in hospital and the diagnosis already made and supplemented by examination of the cerebrospinal fluid. For obvious reasons lumbar puncture was not practicable, but in those cases where it had not already been done the blood was taken and the Wassermann reaction performed.

In the following chapters, devoted to the various aspects of the ætiology, the literature is first discussed and then an analysis made of the information collected from the cases. The results are compared with what is already known; and conclusions are drawn.

CHAPTER I.—AGE, SEX AND CIVIL STATE.

Age.—The age of onset of the disease was noted in fifty-nine of the cases of disseminated sclerosis. This was found to be in accord with the already well-established opinion that it is most common between the ages of 20 to 40. Birley and Dudgeon found in their series of thirty-five cases that the average age of onset was 24·6 years and according to

Collin and Baehr, 88 per cent. of their cases began before the thirty-fifth year. Gowers stated that the disease is met with at all periods of life and especially in the first half of adult life, the majority of cases beginning between the ages of 20 to 35. Below is given a table showing the experience of several writers and including the present work. A graph (fig. 2) has been drawn from these figures and it will be seen that this supports Gowers' contention.

Author	No. cases	0—10	10—20	20—30	30—40	40—50	50—60	60—70
Bing and Reese	272	—	13	92	99	41	20	7
Wechsler ..	194	1	11	65	72	36	8	1
Jelliffe ..	105	9	8	21	27	20	19	1
Present work ..	59	—	6	28	19	4	2	–
Morawitz ..	33	—	7	14	10	21	—	—
Girones ..	10	—	1	6	3	—	—	—
	673	10	46	226	230	122	49	9

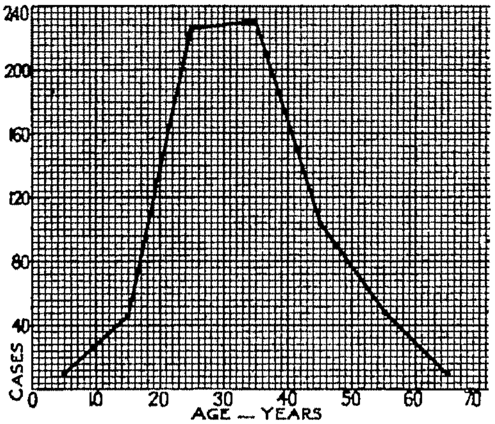

FIG 2.

Sex.—The opinion generally held is that sex has no moment. When small numbers of cases are collected, as a rule one sex predominates. Thus in Girones' 10 cases, there were 8 females and 2 males. Of the 35 cases of Birley and Dudgeon, there were 23 females and 12 males. Blumreich and Jacoby found 23 males and 6 females in 29 cases. Of 60 patients collected in North Wales, 20 were males and 40 females. When larger numbers are considered, it is clear that the disease is fairly evenly distributed between the sexes. To illustrate the truth of this, a total of 4,808 cases has been selected from the literature of various countries. This shows that 2,373 were males and 2,435 females, a proportion of about half and half.

Author			Country		Cases	Males	Females
Wilson	..	..	England and Wales		688	343	345
Grainger Stewart		..	England..	..	1,920	790	1,130
Adams and Blackrock		..	Scotland	..	14	11	3
Foster Coates	..	..	Ireland ..	.	100	61	39
Present work	..	..	Wales ..	..	60	20	40
Blumreich and Jacoby		..	Germany	..	29	23	6
Morawitz..	..	..	Germany	..	33	15	18
Klausner ..	..	..	Germany	..	126	78	48
Dreyfuss ..	..	..	Germany	.	1,151	672	479
Krafft-Ebing	..	..	Germany	..	100	58	42
Bing and Reese	..	..	Switzerland	..	281	117	164
Jelliffe ..	..	..	America ..	.	109	68	41
Wechsler ..	..	..	America ..	..	197	117	80
					4,808	2,373	2,425

Civil state.—Wechsler commented on the absence of statistics on this subject. He found in 186 cases that 63·5 per cent. were married and 36·5 per cent. single. There is no indication whether this referred to their state at the time of examination or at the onset of the disease. Presumably it was the former. This point was noted in 56 of my cases. Thirty-five (62·5 per cent.) were single and 21 (37·5 per cent.) were married at the onset. Taken later at the time of examination, as a result of more marriages, the married proportion was raised to 47 per cent. approximately. In only one case was the onset closely related to marriage. In this (Mrs. Pl.), marriage had been advised for a supposed neurosis, in reality the early symptoms of the disease which were unrecognized until afterwards.

Conclusions.

(1) In the majority of cases the disease begins between the ages of 20 and 35.

(2) Men and women are equally liable to develop the disease.

(3) In this series of cases, more single than married persons were affected.

CHAPTER II.—MENSTRUATION, CLIMACTERIC, PARTURITION.

It is well known that the first symptoms of disseminated sclerosis sometimes begin after parturition. It was thought advisable, therefore, to inquire into the menstrual and child-bearing history of the female patients, to discover if there was any connection between these and the onset of the disease.

Menstruation.—The menstrual history was obtained in 26 cases. In 21, the periods were regular, normal in amount, duration and in the amount of discomfort felt. In 5 cases the following notes were made:—

Case 14*a*.—Sarah J. Menses began at age of 18 to 19 and have always been infrequent and scanty. The onset of the disease was at age of 31.

Case 27*a*.—Mrs. Rob. Before marriage at age of 25 menses were unduly frequent and the loss heavy. After marriage they became normal in character. Onset at age of 28.

Case 37*a*.—Mrs. Wr. Up till marriage severe dysmenorrhœa with prostration, pre-menstrual abdominal colic and vomiting. Onset at age of 11 or 12.

Case 28*a*.—Bella R. Menses irregular, infrequent and scanty until onset of illness at age of 30. Since then they have been normal.

Case 10*b*.—Jenny W. Menstruation began at age of 13, periods irregular at first, in a year or so became normal. Onset of illness at age of 13 about same time as beginning of menstruation.

The climacteric.—The change of life has an effect on the health of many women who tend to develop functional nervous disorders, high blood-pressure, &c., at this time. This point was considered in six of the 34 female cases who had passed the menopause. In three of these the onset of first symptoms bore some time relation to it.

Case 7*a*.—Mrs. El., aged 50, Onset of D.S. four years ago, with sudden blindness and recovery. Recurrence of symptoms a year ago. Periods irregular for past two years, now ceased at age of 54.

Case 34*a*.—Mrs. Und. Symptoms of menopause, i.e., flushings, irregular periods with final stoppage in 1917-18, aged 54. In 1918, after influenza, noticed first symptom of present disease (D.S.)

Case 24*a*.—Mrs. Pr. Onset of D.S. at age of 40. Since then relapses and remissions. Menses normal till age of 44 when had severe menorrhagia. In view of this an artificial menopause was produced with radium at age of 45.

Parturition.—Of 22 married women in this series, 14 had borne children. Parturition had been related either to the onset or to a relapse occurring during the course of the disease in 8. In the remaining 6 it had been uneventful.

(1) *Parturition related to Onset.*

Case 31*a*.—Mrs. Sut. Married at 20. Two years later a son was born. A month or so after this she noticed a weakness of the legs and stiffness (onset). As this occurred over twenty years ago the patient could not be more accurate.

Case 27*a*.—Mrs. Rob. Married at age of 25. No children by design, till became pregnant three years later. Patient states that the present complaint began shortly after this child was born. Labour was conducted under "twilight sleep" and was very successful from an obstetric point of view. The doctor naturally wondered if this process had been harmful and in any way connected with the onset of D.S. The husband, however, recollected what the patient herself had forgotten, that during the early months of pregnancy she had complained of pins and needles in the right arm and leg. These were disregarded until after parturition, when they became more noticeable and were accompanied by weakness of the right leg.

Case 15*a*.—Mrs. Jo. Married at age of 19. A year later a child was born without ill-effects. At age of 24 a second child was born. Shortly after, unsteadiness in walking was noticed and she fell downstairs. She was also very emotional and her husband thought her hysterical. Recovery took place in a month or two. Four years later, when aged 28, a third child was born. Six weeks after parturition weakness of the legs was felt, the speech was indistinct and vision blurred. The patient, her husband and the doctor who attended her throughout are all positive that symptoms did not appear until after childbirth on each occasion.

Case 30*a*.—Mrs. Sp. Married at age of 26. A child was born one and two years after marriage. No ill-effects were observed, but both children proved weakly and died shortly after birth. Aged 30, four years after marriage, gave birth to a third child. A week after parturition had a bad fright (husband became insane) and she noticed weakness of the right leg with stiffness.

Case 9*b*.—Mrs. Wil. Married at age of 22. Has had six children, two of whom are alive to-day, two died in infancy and two were stillborn. The last child was born fifteen years ago, when patient aged 41. Labour was precipitate, the child being born before the arrival of the doctor. There had been no ill-effects after the previous confinements and pregnancy in this last instance was uneventful. Shortly after parturition (two to four weeks) noticed weakness of the legs, particularly of the right.

Case 19*a*.—Mrs. Mat. Married at the age of 28. A year later gave birth to a healthy child. The first symptoms of the present illness were noticed during pregnancy in a mild form and more severely after parturition. They consisted of "pins and needles" in the right leg with weakness and dragging of the right leg (onset).

(2) *Parturition related to Relapses.*

Case 23*a*.—Mrs. Pl. Was single when illness began with sudden blindness at age of 35. Married at age of 36. Three years ago gave birth to a healthy child. During pregnancy her symptoms were less, but after parturition she became worse. She is now pregnant again, and this time is worse rather than better, with retention of urine and paraplegia.

Case 10*a*.—Mrs. Hu. Married at age of 25. Two years later noticed weakness of right leg, which, however, passed off. Aged 32, a son was born, and shortly after this suffered from incontinence of urine and precipitate micturition. This recovered and at age of 40 gave birth to another child. During the puerperium noticed that the sight was blurred and indistinct and that the right leg felt weak.

Parturition causing no Ill-effects

Case 37*a*.—Mrs. Wr. First symptom noticed at age of 11; next at age of 19. Married at age of 22. A child was born a year later, the labour being easy. A second child was born two and a half years after the first, aged 25-26. There was phlebitis of the left leg after this, but no other ill-effects. Neither confinement or pregnancy had any effects on the course of the disease. This did not become chronic and fully established till some years after the birth of the children.

Case 7*c*.—Mrs. Jo. Married at age of 22. Onset of D.S. at age of 27. Two children were born before she was 27 and two since then. Three are living to-day and one is dead. Neither the confinements nor the pregnancies had any ill-effect.

Case 16*a*.—Mrs. Lew Married at 19. She has seven healthy children, aged 26, 25, 23, 21, 15, 9, 7. The present illness began at age of 34, half way through her child-bearing period between the fifth and sixth children. It was unconnected with parturition and the subsequent pregnancies had no noticeable effect on its course or severity.

Case 7*a*.—Mrs. El. Has been married for over twenty years. Has six children and had two miscarriages. Three children are alive and healthy, the other three died in infancy. All the children were born some years before onset of D.S. at age of 50, four years ago. No transitory symptoms were observed at any of the confinements or pregnancies.

Case 34*a*.—Mrs. Und. Married at age of 28. Has two healthy children, aged 30 and 28. Noticed no nervous symptoms before or after birth of these. Onset of D.S. at age of 55, some years after last confinement.

Case 24*a*.—Mrs. Pr. Married at age of 24. A child was born a year later; now alive and well. Noticed no nervous symptoms before or after birth. Onset of D.S occurred at age of 40, many years later.

Summary and Discussion.

(1) *Menstruation.*—This was normal in the majority, in only two out of twenty-six was there a history of scanty and irregular periods. Of twenty-two married women, fourteen had borne children. These facts suggest that there was no defect in their ovarian secretion. There appeared to be no time relation between the onset of the disease and the beginning and cessation of menstruation. This had begun some years before the disseminated sclerosis in all but one case. In this one exception both had started in the same year, and in only three cases was the onset related to the climacteric.

(2) *Pregnancy and parturition.*—Fourteen patients had borne children. No ill-effects were observed in six, but in eight, that is more than half, pregnancy and parturition were related either to the onset or to a relapse in the course of the disease. In some, the first symptoms

were noticed during pregnancy, and in others not until after the birth of the child. The history of Mrs. Rob. suggests that often the first symptoms are unnoticed during pregnancy, and that the disease may be present in latent form before the birth of the child. This is in keeping with the statement of some of those patients who became pregnant after the disease had begun. They noticed that during pregnancy they tended to feel better, but felt worse after delivery. There was no history of difficult labour and the children born were usually healthy.

It is obvious that child-bearing cannot be of first ætiological importance. It can only apply to women, and even so, only a proportion of those who bore children were affected. Also it should be noted that in three cases symptoms followed, not after the birth of the first child, but after the second, third and sixth child respectively. This suggests that some other factor had been added in the interval which had not been present previously. The effects of pregnancy and parturition therefore appear to be auxillary in unmasking a latent condition. This takes place most frequently after parturition, during the puerperium, when the general physical state of the patient may be low.

CHAPTER III.—INJURY, SHOCK AND FATIGUE, EXPOSURE.

These three causes have been grouped together for convenience as they are very similar and are probably the commonest causes given by patients to explain the onset of their symptoms. Leuba is stated to have been the first to note the frequent connection between injury and the onset of disseminated sclerosis. Blumreich and Jacoby, in a careful study of twenty-nine cases, found a history of injury related to the onset in eleven. In nine others there was a history of overwork or shock. Krafft-Ebing found a history of exposure to extremes of temperature in forty out of 100 cases, and concluded that this was an important ætiological factor. Thus one case cited by him was that of a young woman who developed the disease shortly after spending thirty minutes in a cold bath in the month of October! Numerous cases have been described where an accident seemed related to the onset; amongst these may be mentioned the cases of Baldwin, Palmer, Pemberton and Grossmann. Jordan reported a case after an emotional shock; Preissner, another, is a man who had been struck by lightning. The European War of 1914-18 should have furnished numerous examples following injury, shock and exposure, had these factors been important, but in reality records of such cases are rare. Josephy collected thirty-seven cases in soldiers, but found that only in four was there any connection between the onset and an injury received. In only two of these was the connection at all likely.

It is generally agreed to-day, that neither injury, shock nor exposure have any real value as causes of the disease. Grainger Stewart states that it is inconceivable that the pathological changes characteristic of the disease should result from the direct effects of an injury, and he believes that exposure and fatigue probably act in accentuating already existing conditions.

Fifty-six cases of disseminated sclerosis were investigated from this standpoint. The patients were first asked if they could name any likely cause for their illness. If unable to do so, they were questioned about former injury, exposure, shock and fatigue. To act as a control to these results, forty patients who had some other affection of the nervous system were examined in a similar way. The results are tabulated below :—

Injury—Exposure—Shock

Class	Number of cases	Injury given as cause	Previous injury not given as cause	Exposure given as cause	History of exposure not given as cause	Shock given as cause	Over fatigue given as cause	Total	%
D.S. (*A*, *B*, *C*)	56	8	6	3	5	1	1	24	43
Controls (*D* *E*)	40	6	4	1	6	1	1	19	47

From the above figures it is obvious that injury, shock and exposure occur as antecedents in disseminated sclerosis with no greater frequency than in other diseases of the nervous system. In fact, in this series of cases, drawn from the same area and more or less living under the same conditions, these factors were rather less frequently met with in disseminated sclerosis than in other diseases. Personal investigation, combined with the help of relatives under ideal conditions, no doubt accounts for the high figures obtained. It is of interest to note that whereas exposure was given as a cause only four out of fifteen times, injury was cited as a cause in fourteen out of twenty-four instances. This difference is no doubt related to the weighty impression which an injury makes on the mind of an individual as compared to such everyday occurrences as exposure to damp and wet.

In the fourteen cases of disseminated sclerosis giving a history of previous injury, an attempt was made to find out what bearing, if any, this had on the subsequent onset and course of symptoms. The cases were found to fall readily into three groups, and some examples of each are given.

(*A*) *Injury some time before Onset of Symptoms.*

Case 25*a*.—Isac P. At age of 20 was cycling, when his machine skidded and he was thrown violently into a shallow pond of icy-cold water. He was shaken, and felt as if a tight band were round the abdomen, but walked home, a distance of 1½ miles. X-ray is said to have shown a fracture of the spine and the sensation of tightness after persisting for some months was relieved by massage. He kept well till five years later, when at age of 25 the symptoms of disseminated sclerosis first appeared.

This suggests an injury to spinal cord with root pains five years before the onset of symptoms. On examination, there was no evidence of localization of symptoms at site of old injury or signs of compression of cord.

Case 6*a*.—Alan E. Whilst in army, aged 36, fell over a gun limber and broke the left leg. Two years later noticed first symptom of present illness (D.S.), i.e., weakness of the left leg with dragging.

This suggests that the site of a former injury may determine the site of onset of symptoms. The same feature was observed in another case, Robert Jones.

(*B*) *Injury closely related to Onset of Symptoms.*

Case 2*a*.—John A. At age of 20, was walking one stormy night in March on outskirts of Barmouth. Rain and wind being severe, he sheltered under a wall. Whilst there, he was aware of a sudden flash and a bang, and found himself lying on the road, his left leg being twisted under him. On getting up, he found that a chimney on a nearby house had collapsed, damaging the wall he was sheltering under, in its fall. He concluded that he had been struck by lightning. No one else had noticed thunder or lightning that night, and the patient himself admitted that it was the only "bang" and flash he had been aware of. He was badly shaken. His left leg felt numb and weak, though he was able to walk. A few weeks later he had "influenza," which recurred in a month, and after the second attack he noticed double vision and dragging of the left leg. He is now an established case of D.S., and believes that his illness is due to being struck by lightning.

It appears likely that there was no lightning, and that the chimney collapsed owing to the force of the wind. Probably he was knocked down by part of the wall falling on him. The left leg was twisted in the fall. The weakness noticed at the time was not out of proportion to the injury. His illness was ushered in some weeks later by febrile attacks and malaise, described as "influenza." It is more probable that the onset of the disease was related to these attacks, and that its appearance after the injury was purely a coincidence.

Case 1*a*.—Mrs. Al. Aged 43, received a shock whilst adjusting some wires leading to an electric light bulb. The next morning she noticed numbness in the right leg, and a week later had lost the use of the limb. She believes that this was the beginning of her present illness (advanced D.S.). and that it was caused by the electric shock received. On closer inquiry it was found that three months previous to the above events she had been very emotional and depressed, and had had violent tremors of the right arm on attempted movement. Many years before, when aged 22, she had had a bad nervous breakdown following influenza, with weakness of the legs which persisted for several weeks.

(3) *Case* of Rudolf H. described by Grossmann. Grossmann first saw this patient in April, 1905. He showed signs of well-established D.S. and stated that his symptoms had followed closely on an accident in October, 1903, when he had fallen from a height and been taken to hospital unconscious. The man's comrades testified that he had been in excellent health and able for hard work before the accident. Hoping to find a bona-fide case of post-traumatic disseminated sclerosis, Grossmann looked up the original hospital records. He found notes of an examination made a few days after the accident, viz , optic atrophy, nystagmus, intention tremor, forced laughing and unequal knee-jerks. The author concludes that it would have been impossible for such advanced signs to have developed in a few days.

The conclusion seems justified that this patient was suffering from the disease in a latent, though advanced form. His faculties were not impaired until after the accident, which served to unmask the latent disease.

(*C*) *Injury a Result rather than a Cause.*

(There were numerous examples of this.)

Case 24*a*.—Mrs. Und In October, 1919, when out walking, slipped and fell on asphalt pavement, injuring the right knee. After this accident she noticed that the legs felt weak and she dates her illness from it.

On inquiry it was found that in August, 1919, the patient was lame in the left leg for a month or so.

It is probable that the patient fell because her legs were weak and that the injury resulted from weakness of the legs rather than the reverse which she alleged.

Conclusions.

(1) A history of injury, shock or exposure was often met with in the fifty-six cases of disseminated sclerosis examined, but not more frequently than in a control series of forty cases of other diseases of the nervous system.

(2) In some cases, where a part had been injured some time before the onset of symptoms, the disease appeared to affect the function of that part first.

(3) In other cases there was a close connection between an injury

and the first recognition of symptoms. Though often given causal value by patients this apparent relation is more probably due to:—

(*a*) Forgetfulness on the part of the patients of earlier symptoms.

(*b*) The injury being the result rather than the cause of symptoms.

(*c*) The disease being present in latent unrecognized form before the injury, the latter serving to draw attention to it.

(*d*) Coincidence.

CHAPTER IV.—THE INFLUENCE OF HEREDITY.

Formerly, disseminated sclerosis was considered by many to be a primary degenerative process. Thus Strümpell thought it was a multiple gliosis dependent on congenital influences. Müller was of the same opinion, being unable to find an external cause in the majority of his cases. In modern times, one of the few remaining advocates of the older view is Hassin. After a careful examination of pathological material from thirteen cases, this worker came to the conclusion that the essential cause was a degeneration of myelin and that there was no evidence of an inflammatory process.

From the standpoint of ætiology, it is clear that if the disease is a primary degeneration, search for external causes will not be of much value. At the most, such effects could only be contributory or secondary. A primary degeneration suggests a congenitally weak or unstable nervous system. The causes of this are more likely to be found in the family history of the patient. One might expect frequent instances of the disease in members of the same family, an early age of onset and a neuropathic inheritance. Furthermore, it might be possible to recognize certain distinctive physical types as being especially liable to develop the disease. The present series of cases was investigated along these lines.

Familial Incidence.

The number of familial cases reported in the literature is small. Eichhorst, Reynolds, Batten, Allen, Robinson and Abrahamson have contributed examples. The cases described by Eichhorst in 1896 and 1913 were confirmed by autopsy. They are probably the most convincing in the literature. A brief summary of them is given below:—

(1896).—Case of a woman with weakness of legs, tremor, scanning speech, nystagmus and pallor of discs. Two years after onset a son was born who subsequently developed similar symptoms. At autopsy, in each case, small sclerotic patches were found scattered throughout the spinal cord.

(1913).—Mother and son with symptoms of spastic paraplegia. At autopsy, grey patches varying in size were found in the brain and spinal cord.

Many writers, notably Cestan and Guillain, Ferguson and Critchley, have described familial diseases closely resembling disseminated sclerosis. The last-named authors described a family in which thirteen members were affected, the clinical picture varying from that of paralysis agitans to disseminated sclerosis. The inference is that many familial diseases, which are certainly not disseminated sclerosis, closely mimic it in their clinical features. For this reason many of the so-called familial cases, which were formerly accepted and lent support to the hereditary view, are now discredited.

Only four cases were reported in North Wales. Two of these were in a brother and sister. The sister's case was obscure and had at one time been diagnosed as disseminated sclerosis. *Case* 13*e.*—Barbara H.. On examination it appeared more probable that the condition was due to the after-effects of encephalitis lethargica. The brother (*Case* D(5), William H.) showed a spastic paraplegia, and syphilis had been excluded. Two more probable cases were found in sisters. On clinical grounds these presented typical features of disseminated sclerosis. One of them was living in North Wales and was examined personally. The main features are given below. Except for these two no other familial cases were found in North Wales.

Case 32*a.*—Bessie T., aged 43 (examined personally). At age of 18 sudden blindness left eye and right vision blurred, recovering completely in right eye, only partially in left. Aged 30, noticed left foot dragging and sensation "as if a cat were rubbing his back against the leg." This lasted one to two months. Aged 32, had nervous breakdown, apprehensive and emotional. At age of 35, lameness left leg which has persisted since and has spread to other leg and to the left arm. *On examination*: temporal fields of vision reduced with pallor of discs. Intention tremor right and left. Spastic paraplegia, right greater than left. Tendon reflexes +, ankle clonus and extensor plantars, absent abdominals. Difficulty in retaining urine and constipation. Wassermann reaction negative.

Case 14*c.*—Nellie T., aged 41 (from notes). At age of 23, "neuritis" in left arm. Aged 32 numbness of legs, the right one being weak. Treated in Guy's Hospital. Wassermann reaction negative in blood and C.S.F. Diagnosis of disseminated sclerosis. Recovered partially but at age of 35 lost control of bladder. Admitted Liverpool Royal Infirmary—cranial nerves normal, no speech defect or intention tremor. Knee-jerks +++, ankle and patellar clonus, extensor plantars, absent abdominal reflexes. Recovered and kept well till age of 38, when both legs affected with weakness. Since then has been a semi-invalid.

Early Age of Onset.

Strümpell and Oppenheim believed that the disease could be traced in its beginnings to early childhood. If so, this would strengthen the primary degenerative view and bring the disease into line with other congenital affections. Recently Wechsler has made an excellent review of the subject and concludes that the majority of so-called cases in children are based on insufficient evidence; that such cases are in reality often examples of other diseases, such as Friedreich's ataxia, congenital lues, Little's disease, family spastic paralysis and the after-effects of encephalitis lethargica. In his own series of 197 cases he found only four in children. He concluded, therefore, that whereas undoubted cases do occasionally occur in childhood, such are extremely rare.

It is difficult to decide what may be the first symptom in a given instance. For example, in No. 37*a*, Mrs. Wr., of this series, there was transient numbness of the left leg at the age of 11, and not till 19 was the next symptom, temporary blindness, noticed. If the plan is adopted of noting all possible nervous symptoms from childhood onwards, full justice will be done to the theory of beginning in early life. In fifty cases it was possible to do this fairly closely. The judges of former fitness were the family doctor, the parents, brothers and sisters. In forty-two (84 per cent.) the patients appeared to have been in robust physical and mental health until the onset in adult life. In only eight (16 per cent.) was there a history of nervous symptoms in childhood. In only two could the onset be fairly placed before the age of 15. Details are given below:—

Case 29*a*.—Joseph R. Always nervous and sensitive. Stammering a feature of early life. Onset at age of 26.

Case 37*a*.—Mrs. Wr. Aged 11 noticed numbness of the left leg, which lasted one week. Did not do anything about this, and was otherwise well till aged 19, when became temporarily blind (onset).

Case 5*a*.—Winifred E. As a child was always unduly sensitive; "felt things more than others." Was shy, conscientious and hard worker. Onset at age of 30.

Case 14*a*.—Sarah J. As a child and up till onset in adult life always "delicate," readily tired by exertion, over-sensitive and unduly apprehensive.

Case 20*a*.—Marjorie O. Parents state she was the most "nervous" child of the family. Was always "highly strung," very sensitive and kept her own company. Easily frightened and shy of strangers. Strong physically. Onset at age of 20.

Case 5b.—Nesta R. As a child was always nervous, readily frightened, shy and over-conscientious. Onset at age of 23.

Case 21a.—Cassie O. Always unduly sensitive, more reserved and shy than other members of the family. Physically strong. Onset at 20.

Case 10b.—Jenny W. From earliest childhood shy and sensitive. Robust physically. Aged 13 noticed diplopia and weakness left side of face (onset).

Neuropathic Inheritance.

Gowers held that an indirect neuropathic inheritance was fairly common in disseminated sclerosis. Krafft-Ebing found seventeen out of 100 cases in which the family history showed drunkenness, insanity, migraine and other examples of nervous disease. Steiner, on the contrary, believes that nervous and mental diseases are no more common in the relatives of cases of disseminated sclerosis than in those of healthy individuals.

In forty cases the family history was investigated closely. In fourteen (35 per cent.) there was a history of nervous or mental disease in other members of the same family.

Case 34a.—Mrs. Und. Father died of apoplexy and two brothers were alcoholics.

Case 37a.—Mrs. Wr. One brother suffered from severe shell-shock during war.

Case 4a.—Mrs. Bar. One sister has had nervous breakdowns and is of a highly excitable type. Her daughter (niece of patient) has had melancholia, now recovered.

Case 24a.—Mrs. Pr. Two first cousins affected; the one with a temporary paraplegia lasting a year (? disseminated sclerosis), the other with a nervous breakdown.

Case 20a.—Marjorie O. Paternal grandfather died of apoplexy, maternal grandfather of paralysis agitans; an aunt suffers from fits.

Case 5a.—Winifred E. Mother hemiplegic as result of several strokes.

Case 29a.—Joseph R. One sister neurasthenic; had chorea as a child. Another sister died from melancholia, "refused food and withered away" (? anorexia nervosa).

Case 21a.—Cassie O. One brother an epileptic; fourteen in family, patient thirteenth; last child died infancy.

Case 9a.—John H. One sister suffers from neurasthenia

Case 7a.—Mrs. El. One brother died tabes dorsalis.

Case 10a.—Mrs. Hu. Father died of apoplexy. One sister has weakness in the legs from time to time. All brothers and sisters "very highly strung."

Case 32*a*. Bessie T. One brother an epileptic. One sister symptoms suggestive of disseminated sclerosis.

Case 22*a*.—Jane O. Father died aged 71, "very nervous." One brother suffers from periodic depression. One sister is melancholic.

Case 2*c*.—Mother suffers from paralysis agitans.

Type of Person affected.

Charles Dana states that he has never seen a case in an obese subject and Davenport suggests that it is the tall northern or Scandinavian races in America who appear to be most liable.

Notes were made in these cases of the physical characteristics, whether tall or short in stature, bodily nutrition at the time of onset and whether the patients were of the dark or fair haired type.

Height.—In 47 cases, 33 were of average height, 10 were tall in stature (women over 5 ft. 8 in., men 6 ft. or over) and 4 were below average height. Thus, in this series, persons of average height were most commonly affected, but tall individuals were twice as common as short ones.

Nutrition.—In 46 cases, 24 were of average nutrition, 20 undernourished and of the "asthenic" type and 2 obese. Undernutrition was therefore unduly prevalent at the time of onset and obesity rarely found.

Type.—In 47 cases, 33 belonged to the dark haired and complexioned type and 14 to the fair haired type, the dark types outnumbering the fair by about 2:1. Dark types are however commonly met with in North Wales.

Place in family.—In 34 cases, the birth relation to other brothers and sisters was noted. In only 1 case was the patient an only child. Four were the eldest and 6 the youngest members of their respective families. Eight belonged to the first half and 19 to the second half. The only point of note is therefore the apparent tendency in this series of the younger or more junior members of large families to be affected.

Summary and Comments.

(1) *Familial incidence.*—Authentic records of familial cases are rare. Only two examples in sisters were found among sixty-five cases.

(2) *Alleged early onset.*—The majority of so-called cases in children are not disseminated sclerosis. In only two cases in this series did the disease begin in childhood. In the great majority, there were no

nervous symptoms of any kind, until the onset in adult life, the persons affected having been previously healthy subjects.

(3) *Neuropathic inheritance.*—Nervous and mental diseases were found in the families of 14 out of 40 cases (35 per cent.), the former 10 times and the latter 15 times.

(4) *Special physical type.*—No one type was found but the disease appears to be more common in thin persons, and dark types outnumbered the fair by 2 to 1. This latter proportion, however, is probably true of the district as a whole. Tallness of stature was twice as common as shortness. Of 34 cases, 18 were among the last born in their respective families and 8 among the first born.

There is little, therefore, on ætiological grounds, to support the view that disseminated sclerosis is due to a primary degeneration dependent on congenital hereditary influences. Instances of its occurrence in families are rare and its beginnings cannot be traced to early life. It appears however that those who are affected with the disease frequently come from families which show a liability to nervous and mental disease in general. This, of course, is no more than may be said of many other diseases, both infective and degenerative, which show the same tendency to run in families.

CHAPTER V.—RACIAL AND GEOGRAPHIC DISTRIBUTION.

Disseminated sclerosis is not a notifiable disease, and it is therefore not possible to obtain exact information of its incidence in the general population. Wilson found, however, that in 1925, 688 persons died from the disease in England and Wales. Steiner believes that after neurosyphilis disseminated sclerosis is the commonest organic disease of the nervous system. Through hospital returns one can assess its frequency among other diseases. Thus Williamson found that during ten years at the Manchester Royal Infirmary 2,294 cases of nervous disease of all kinds were treated, and that of these 61 were disseminated sclerosis (2·7 per cent.). Grainger Stewart was able to collect information of 1,920 cases from the records of the National Hospital, Queen's Square, where only nervous diseases are treated; 10 per cent. of the annual admissions were disseminated sclerosis.

The geographic and racial distribution of the disease has for long been a subject of discussion. What evidence there is points to a selective rather than a free distribution of the disease throughout the world. The work which has been done on these lines will now be discussed.

(a) *Racial Distribution.*

(1) *Infrequency of disseminated sclerosis in America.*—Early in the present century the suggestion was made that the disease was more common in Europe than in America. Thus in 1903 Bramwell concluded, from a comparison of his own cases with those of contemporary American writers, that it was three and a half times more common in England than in America. Among 2,760 hospital patients with general nervous diseases he found 1·8 per cent. cases of disseminated sclerosis. Jelliffe, on the other hand, among 21,502 cases found only 104 or a rate of 0·3 per cent. These figures are typical of those given at this period. Collins and Baehr, writing in 1914, referred to the possibility that the apparent infrequency in America was due, not so much to rarity, as to differences in diagnostic criteria, many cases being labelled disseminated sclerosis in Europe which would not be so called in America. It is to be noted, however, that their findings of only 91 out of 12,000 cases (0·75 per cent.) supported the general contention.

Light has been thrown on this subject more recently from a different angle. Pearce Bailey has written an interesting paper on disseminated sclerosis in American military recruits during the war. A total number of 6,916 cases of organic nervous disease was reported, and of these 511 had disseminated sclerosis. The rate for disseminated sclerosis among nervous diseases as a whole, functional and organic, was 0·74 per cent., almost the same as Collins and Baehr's figure. "The average of foreign-born (Europeans) in the whole group of organic conditions was 9·2 per cent., while in multiple sclerosis it was higher, 12·7." This seems to indicate that the disease is less common in native-born Americans than in Europeans. It is of interest to note here that Jelliffe, writing nineteen years before, found among his 109 patients that more than half were European-born.

(2) *Frequency in Europe.*—The greater part of the literature on disseminated sclerosis has been contributed by France, Germany and Great Britain. The large bulk of this is in itself evidence in favour of the frequency of the disease in these countries. Monrad-Krohn states that it is common in Norway. In 1926 Bing and Reese published the results of a survey of north-west Switzerland for disseminated sclerosis. They collected 950 cases and calculated that this would give a rate of 1 in 3 or 4,000 of the population. These results have suggested to some that the disease is especially prevalent in Switzerland. Before this conclusion is drawn it should be remembered that we have nothing

of a similar kind with which to compare these results. The present investigation in North Wales is, however, directed along similar lines. Excluding the six cases from Ruthin Castle and two from Liverpool there remain 57 (in Classes A, B and C) which were found in this area which has a population of 489,270. This gives a rate of about 1 case per 8,600 of the inhabitants. The writer's feeling is that this number is probably an under-estimate. Adams has found disseminated sclerosis a common organic disease of the nervous system in the West of Scotland, and Foster Coates has referred to its frequency in the North of Ireland. He found 106 out of 728 cases of nervous disease treated in the Royal Victoria Hospital, Belfast, in three years (14·5 per cent.). This is the highest rate which has been recorded

American writers have been able to draw reasonable conclusions as to its relative frequency among the various European races. Thus Pearce Bailey, already referred to, found among his foreign-born recruits that disseminated sclerosis was most frequent in Scandinavians (12·5), in French next (10·7), Slavs (9), Germans (8·3), Scotch (8·2), English (8·1) and Irish (7·9). In the other races the incidence was much lower. These results have been supported by Davenport, who noted the birthplace of seventy foreign-born cases in New York. He found that the English and Germans had about twice as many cases as might be expected, the Irish slightly more and Scandinavians three times the number. The Italians were far below expectations. Jelliffe also found that among his foreign-born patients Germans and British predominated.

(3) *Frequency in eastern and tropical countries.*—Steiner states that a South American neurologist informed him that the disease is rare in that continent. Miura, speaking at a German Congress in 1911, commented on the few cases he had met with in Japan. Sprawson, who worked in India for twenty-seven years, had not seen a single case in a native, though he had come across two cases in Europeans resident in India. This experience, however, was not shared by some of the other speakers at the conference where the discussion took place.

(4) *Distribution of cases in explored areas.*—In no part of the world does disseminated sclerosis occur endemically, and it is difficult to draw conclusions about the natural conditions under which it is most liable to develop. Davenport made a map of the United States to show the incidence of it in the various States. This was based on knowledge of the homes of military recruits, rejected on account of the disease. He found that cases occurred with greatest frequency in the States of

Minnesota, Michigan and Wisconsin. He noted that these States bordered on the great lakes and are inhabited largely by Scandinavians and their descendants. Bing and Reese also published a map of north-west Switzerland plotting the cases found on it. There was nothing remarkable about the result. Wilson noted the place of death of 688 persons who had died from the disease in 1926 in England and Wales. The maximum incidence was found to be in Peterboro', Merioneth, Monmouth, Cardigan and Cornwall. These are mainly rural districts, and except the first named have a sea coast. The writer has been unable to substantiate the claims of Merionethshire. He found the disease in this county not more frequent than in the others.

In this work, the cases found in North Wales were plotted on a large-scale map, a black dot representing each case. The number charted was forty-seven, the remaining cases having to be omitted for various reasons. In forty the disease began and the patients lived within the confines of North Wales. Six cases occurred in the Wrexham area, four near Bala in Merioneth, along the valley of the river Dee, and five in the coastal area around Llandudno and Colwyn Bay. There was no congregation at any one point. Except for the Bala district the other parts have a fairly dense population, and are places where, in the ordinary course, one might expect to meet with a fair number of cases. Ten cases occurred in Anglesey. This seems a large number for a small area and thinly-populated county. The population of Anglesey forms about 10 per cent. of the total for North Wales, whereas 25 per cent. of the forty cases were found there. This frequency in Anglesey is not due to any special facilities for investigation there. Indeed, as it was the most distant part from the centre of the inquiry, it was the least accessible. It is probable that the number of cases found there is an underestimate. This finding may or may not be related to the geographic features of the county, Anglesey being a flat open country with no part much raised above sea level.

Summary and Comments.

Though cases have been reported from recognized centres all over the world, Europe appears to be chiefly affected, and particularly Great Britain, France, Germany, Scandinavia and Switzerland. The disease is less common in North America than in Europe. What little is known suggests that it is rare in tropical and Eastern countries. It may be said, therefore, to occur most frequently in northern latitudes and temperate climates. In North Wales cases were found scattered along the lines of thickest population, but Anglesey, which is a low-lying, flat open district, had a larger proportion than might have been expected. The rate found was about 1 in 8,600 inhabitants.

CHAPTER VI.—RURAL AND URBAN INCIDENCE.

Is disseminated sclerosis more common in country districts than in towns and cities? Several observers have recorded their impressions. Grainger Stewart believes that the disease is met with as frequently in industrial and urban areas as in rural districts. Müller found that most of his cases (from Strümpell's Clinic) came from the country and Morawitz, working at Tübingen, found that it was the commonest disease of the nervous system in the Würtemberg country district. Steiner thinks that it is much more a disease of the country than of the town, and that when it occurs in town dwellers inquiry will often show that they formerly lived on the land. Adams is a supporter of the same view, and finds that the majority of his patients come from the country as opposed to the town.

These views show that there is a strong bias in favour of the country incidence. It will be observed, however, that individual impressions are apt to be coloured by the nature of the district in which they are made. Granted that disseminated sclerosis is probably one of the commonest organic nervous diseases in the country, we require further evidence to prove that the disease is actually more frequent there than in towns. Recourse must be had to the method of investigating a given area if this point is to be decided. The total population and the ratio of urban to rural dwellers should be known. By contrasting the dwelling-places of the cases found with these facts a true estimate can be formed of the distribution of the disease in the area. Some work has already been done on these lines and in this study the same method has been adopted.

In the United States C. B. Davenport found a defect rate for disseminated sclerosis among recruits of 10 in 100,000 of the population examined. The urban rate was 12 in 100,000 and the rural 8 in 100,000. He concluded, therefore, that the urban rate for the disease was one-half greater than the rural rate.

In Northern Ireland Foster Coates collected 100 cases from the records of the Royal Victoria Hospital, Belfast. He found that two-thirds were town and one-third country dwellers. Now 10 per cent. only of the general hospital population came from the country. This suggested that the disease was more common in the country. On looking over these figures, however, it is difficult to escape from the fact that two-thirds of his cases were town dwellers.

Bing and Reese in a survey of north-west Switzerland found the largest rate (7·4 in 10,000 inhabitants) in Basel City. On examining the excellent tables given one is struck by the small rate for cases in areas of small population—presumably rural areas. The greatest rate appears to be in the more thickly-populated areas. The author's only comment on this point was that the greater frequency of the disease in Basel may have been due to the improved facilities for diagnosis existing in cities as compared to country districts. The Swiss results certainly do not indicate that the disease is unduly prevalent in rural districts.

Else Koch in a recent paper has noted the place of birth and dwelling of 700 German military war pensioners invalided because of the disease. Figures were given which showed the distribution of the German population over urban and rural areas. By "rural" was meant districts having a population of under 2,000 inhabitants. From these figures it is evident that approximately 45 per cent. of the total population may be classified as rural and 55 per cent. as urban. Koch found that 425 of the pensioners (60 per cent.) were born in rural and 275 (40 per cent.) in urban districts. This showed a preponderance in favour of the country for birth-place. When the dwelling-places of the 700 pensioners were considered it was found, however, that more came from towns than from the country (301 rural, 43 per cent., and 379 urban, 57 per cent.). Though Koch attributes this to the tendency of the population to migrate to cities in recent years, and evidently believes that the disease is essentially a rural one, there appears to be little to support her contention from the above figures.

In investigating the subject of rural and urban incidence in North Wales forty-five cases were available. The same plan of noting the birth and dwelling place was followed, and in addition the place of onset was noted.

Place of Birth.

Twenty-five cases were born in the country or in villages, whilst twenty were born in towns, cities or industrial areas.

Persons born in country or village .. .. .. = 25 cases
" " industrial areas and small towns .. .. = 5 "
" " large towns or cities .. .. .. = 15 "

Places lived in during Life.

Though there was a small number who had moved about from place to place, the majority of patients had spent all their life either in towns or in the country. Special inquiry was directed towards ascertaining whether or not the patients had at any time lived or worked on a farm or in the country. The results were as follows :—

Persons who had always lived in the country or on farms .. = 20 cases
,, ,, always lived in towns or industrial areas and had never worked or lived in country or farm .. .. = 17 ,,
,, ,, lived both in town and in country .. = 8 ,,

The country dwellers predominated; 28-45 (62 per cent.). Nevertheless the number of patients who had always lived in towns is striking and the difference between the two groups is not great.

Place of Onset of Disease.

In determining the place of onset of the disease, it was an advantage that in this series of cases thirty-seven out of the forty-five investigated had always lived in either town or country and many always in the same place. In a few the onset had followed shortly after a change of dwelling. These were omitted to avoid confusion.

Persons living in country or in a village at onset .. .. = 25 cases
,, ,, towns at time of onset .. .. .. = 20 ,,

Thus after considering the places of birth, dwelling-places and sites of onset, there is no indication that the disease occurs more commonly in country dwellers than in town dwellers. The distribution between urban and rural districts is approximately equal with a slight preponderance in favour of the country. This corresponds closely to the distribution of the population as a whole in the area investigated.

SUMMARY.

	Urban	Rural
Place of birth	44 per cent.	56 per cent.
Dwelling place	38 ,, ,,	62 ,, ,,
Onset	44 ,, ,,	56 ,, ,,
General population	42 ,, ,,	58 ,, ,,

It is clear that the distribution of disseminated sclerosis in North Wales closely follows that of the general population. There is no evidence to suggest that it is more commonly met with in the country than in towns and industrial areas. This conclusion appears to be in keeping with that of other workers who have adopted similar methods of inquiry.

Judging from the statements of doctors in practice the disease does not appear to be unduly prevalent in the province. The majority have seen one or two cases at some time or another, but a number deny its existence in their districts entirely. A large number said that they had found encephalitis lethargica and its after-affects a more common disease. At a rough estimate, had this inquiry concerned the latter, 100 to 150 cases might have been collected. Neurosyphilis appears to be as uncommon here as in other rural areas.

CHAPTER VII.—OCCUPATION.

Literature.

(1) *Industrial causes.*—The possibility that occupation might have some connection with the ætiology of disseminated sclerosis was originally suggested by Oppenheim. He found the disease common in lead, copper and phosphorus workers, in engravers, lithographers, and those working with aniline dyes. Oppenheim's views, however, have not received general support and the opinion of most writers to-day is that metallic poisoning plays little or no part in the ætiology of the disease. McGurn reported two cases in young men following carbon monoxide poisoning. The first showed, three and a half years after exposure, scanning speech, nystagmus, failing vision, exaggerated tendon jerks, ankle clonus and extensor plantar responses. In this case there was a convincing relationship between the exposure to CO fumes and the onset of symptoms. The description of the second case raises doubt as to the diagnosis. Recently, Helpert described a case following CO poisoning and has given a good review of the literature bearing on this subject. Such examples are undoubtedly rare.

(2) *Farming and agricultural work.*—Hoffman found a large proportion of his cases, 37 to 100, among farm workers, but concluded that the type of occupation depended largely on the local conditions surrounding the hospital or clinic where the observations were made. Adams finds that the occupations most common in his patients are farming, wood-working, game-keeping, gardening and byre-keeping. Foster Coates analysed the occupations of 100 hospital patients in Northern Ireland. He found 17 labourers, 19 household workers and 10 farmers. The percentage of farmers in the general hospital population was 3 per cent. and he concluded therefore that the 10 per cent. farmers found in disseminated sclerosis pointed to a prevalence of this occupation in the disease. Wilson investigated the occupations of 688 persons who had died in England and Wales in 1925. After classifying the occupations, the actual number of deaths in a given occupation were compared with the expected deaths. Farmers, for example, in whom the expected death-rate was 7·46, showed an actual

death-rate of 16, a difference of 8·54. None of the other occupations showed a greater variance between expected and actual deaths than 3 at the most. The total number of deaths in farmers, farm labourers and their relatives or dependants was 56, not a large proportion of the 688, but nevertheless the greatest number of deaths in any one occupation recorded. Bing and Reese, in their survey of Switzerland, noted the occupations of 281 persons; 29 were factory workers, 27 agricultural workers and 110 were engaged in household duties. Industries and trades outnumbered agricultural workers by 52 to 27. They were therefore unable to support the alleged frequency of the disease in farmers and agricultural workers.

(3) *Wood-workers.*—The most comprehensive work on the subject of occupation has been done by three German workers, Dreyfuss, Barnass and Koch. In 1921, Dreyfuss collected 1,151 cases (648 from the literature) and found a preponderance for rural occupations (Landwirtschaftberufe). He admitted in all fairness, however, that this finding was not of much value in itself, as in most countries the number of persons engaged in rural occupations is usually high; 672 of the cases were manual workers and he went into this question more closely. The frequency of a given occupation in 1,000 of the population was contrasted with the frequency of a given occupation in 1,000 cases of disseminated sclerosis. By this method he found a preponderance in favour of joiners and cabinet makers (+ 7·8). This was the highest figure noted in a long series of occupations given. Tailors were + 5·7 and painters + 5·4. The frequency in tailors is explained on the possibility that this occupation, requiring less physical effort, may be taken up on the appearance of early signs of the disease. The same reasoning, however, cannot be applied to painters! Dreyfuss divided the manual workers into three classes: wood-workers, metal-workers and building trades. By the same comparative method, he found an overwhelming preponderance in favour of wood-workers (+ 21·3), the building trades being + 12 and the metal-workers − 36·3. Barnass and Koch's conclusions in finding a frequency in wood-workers are very similar. Like Dreyfuss, they were unable to conduct a personal investigation but relied on the information supplied by the pensions papers of 700 military invalids suffering from the disease.

Present Work.

The occupations of 58 persons suffering from disseminated sclerosis were investigated. The total number of cases is too small to draw direct conclusions from, and some consideration must be given to the general frequency of various occupations in the district. Some comparative method was necessary to find out if there was any true frequency of the disease in certain occupations more than in others. The method adopted was to compare these results with the occupations found in 40 other "control" cases living in North Wales. It was thus possible to contrast the frequency of various occupations in the two groups and decide if any particular one occurred with greater frequency in disseminated sclerosis than in other diseases.

Many of the patients gave more than one occupation. Thus, *Case 9a*, John H., had been a grocer's assistant until 1914. He had served in the war as a soldier and returned afterwards to work in a slate quarry. His illness began when he was in the army. Some patients followed two or more occupations simultaneously. Thus, *Case 4b*, Lloyd J., was a builder by trade but lived and worked on a farm and mended boots and shoes in his spare time. It was not possible to differentiate between these various occupations and decide which was important and which not. All were recorded so that they should have their full significance

The results are set out in the accompanying table. In column (1) the various occupations (83) followed during the course of the lives of 58 cases of disseminated sclerosis are noted. In column (2) the same procedure is adopted for the 40 controls (57 occupations). In column (3) the occupations (60) pursued at the time of onset of disseminated sclerosis are noted.

Occupation	(1) Various occupations followed during life. 58 cases D.S.	(2) Various occupations followed during life. 40 cases "controls"	(3) Actual occupation at onset. 58 cases D.S.
Domestic work	29	24	18
Agricultural work (farmers, gardeners, labourers, &c.)	12	11	8
Teaching	8	4	3
Shop workers	7	5	7
Soldiers	6	2	3
Clerical workers (clerks, typists, secretaries, &c.)	5	1	5
Hotel and restaurant workers ..	4	1	3
Quarrymen	4	3	5
Factory workers	2	0	5
Building trades	2	2	1
Students and pupils	4	4	2

Domestic workers head the list. This is of no special significance when taken into account with the preponderance of females in the series of cases.

Land-workers formed about 14 per cent. of the various occupations given in disseminated sclerosis (12 out of 83) and about 19 per cent. of the occupations of the control cases (11 out of 57). 13 per cent. had been working on the land at the time of onset of the disease. These figures do not suggest that farmers as a class are more prone to develop disseminated sclerosis than other diseases of the nervous system. In the report of the Medical Officer of Health for the County of Caernarvon it is stated that 7,965 of the male population of 45,249 were engaged in agricultural work. This works out at about 18 per cent. and closely corresponds to the above figures.

Teachers.—Eight times out of 83 (about 10 per cent.) represents the frequency of this occupation in disseminated sclerosis and 4 times out of 57 (7 per cent.) in the controls. This suggests a prevalence of disseminated sclerosis among teachers but it should be noted that only 5 per cent. were actually employed in this work at the time of onset of the disease. Again, teaching is a fairly common occupation in North Wales on account of the large number of schools in the area.

Clerical workers.—Five out of the 83 occupations given in disseminated sclerosis were clerical (6 per cent.) At the onset of the disease the number was 5 in 60 (8 per cent.); in the controls clerical work was mentioned once in 57 times (2 per cent.). In Caernarvonshire, approximately 2·3 per cent. of the population is engaged in clerical work. There is some evidence here, therefore, to suggest that clerical workers are more prone to develop the disease.

Wood-workers.—In view of the attention which has been given to this subject special inquiry was made for work with wood in all cases. Only one case occurred however in the whole series (*Case* 10 *c*, Stephen J., a joiner).

Other occupations.—These showed nothing of significance and tended to follow the general distribution of occupation in the population as compared with the controls.

Summary and Comments.

(1) A comparative study has been made of the occupations of fifty-eight cases of disseminated sclerosis and forty cases of other diseases of the nervous system found in North Wales.

(2) No evidence has been found to show that the disease is unduly prevalent in wood-workers or farmers, or more commonly met with in the agricultural classes than are other diseases of the nervous system.

(3) The occupations of teaching and clerical work were noted to be more common than might be expected.

CHAPTER VIII.—LIVING CONDITIONS.

The work under this heading was divided into three portions :—

(1) To search for cases occurring in the same house, village, town or district.

(2) To inquire for certain alleged factors.

(3) To inspect the living conditions of the cases found.

(1) *Cases occurring together.*—In the sixty-five cases investigated none were found living in the same house, street or district. In some of the towns such as Mold, Holywell and Colwyn Bay, two to three cases were reported, but this had no significance. The patients had migrated from other places widely apart after the disease had begun. A case was seen in Ponkey, near Wrexham (*A* 15, Mrs. Jo.) and shortly after another obscure nervous disease was reported living next door (*E* 35, William S.). On examination however this was thought to be probably encephalitis lethargica, and the hope of finding adjoining cases of disseminated sclerosis had to be abandoned.

(2) *Inquiry for certain alleged factors.*—Steiner found a history of insect bite and particularly tick-bite in many cases and believes this to be of importance. Ticks appear to be more common on the continent of Europe than in the United Kingdom, judging from the statements of farmers. Though most sheep and other animals such as dogs and cattle may harbour ticks in their wool or hair, farm workers in this country are not often bitten. Only two gave a history of insect bite. Wilson suggests the rat as a possible source of infection and found a history of bathing, immersion or working in rat-polluted water in many of the persons examined by her. In deference to this view leading questions were put to forty-five cases of disseminated sclerosis (Classes *A* and *B*) concerning rats. Positive replies were received from only thirteen and nine of these were farm workers who were likely to meet with the vermin in the course of their work. The usual statement was rat-infested dwelling house or farm premises with a few instances of polluted water supply.

This finding may be compared with the control cases. Similar questions were put to forty persons in Classes *D* and *E*. A positive history of living in contact with rats was obtained in twelve.

(3) *Living conditions.*—It was felt that only those patients who had spent their lives in one place or under the same conditions were suitable for investigation. It is probable that little is to be gained from a study of those who have moved from place to place and lived under

varying conditions. Nothing short of a life history would suffice, and even then the difficulty would arise of deciding what was important and what was not. In North Wales, only ten cases of disseminated sclerosis were found which answered to these requirements. These persons had dwelt in the same house or district before and after the onset of the disease, often in small isolated communities, where the conditions were simple and relatively easy to study. These places were visited and inspected, and the information obtained supplemented by the patient's doctor or relatives. The following points were noted :—

(1) Natural features of the neighbourhood.
(2) Type of house, subsoil, accommodation, sanitation.
(3) Water supply.
(4) Routine of life and work.

Case A 7.—Mrs. El. Has lived in the same house in a small town on the sea coast of Anglesey for twenty-six years. Indoor life. Housework. Good house. Water supply from a shallow open well on the cliffs nearby. On the hillside, about 10 to 15 yards above the well, is a large stagnant pool of rain water, no doubt supplying the well by filtration.

Case A 8.—Mrs. Fl. Was born and has lived all her life at present address in small town in an industrial district in Flintshire. Good terrace house. Water supply from town mains. Father and brothers coal miners, and husband a fitter in engineering works. Housework, and lives mostly indoors.

Case A 12.—Price J. Born and lived all his life in a village in Carnarvonshire, situated in an inland valley enclosed by mountains. Large cottage type of house, part shop. Dry sanitation. Water supply by mains from small reservoir in hills. Formerly from well. At onset of illness worked as slate quarryman.

Case A 21.—Cassie O. Born and lived all life in same house in a sea-coast village in Anglesey. House almost on seashore in exposed situation, well built. The water supply is peculiar in that the house has its own well under the floor of the backyard. The other houses in the village are supplied with tap water from the mains. Housework.

Case A 38.—Alex. W. Has lived in Llandudno in same house for twenty years. It is a small cottage wedged in between others in a back street behind a large hotel on sea front. Interior naturally dark and damp, rooms small and badly ventilated. Water supply from town mains. Labourer on odd jobs in town.

Case A 39.—Owen W. For past seventeen years has lived with parents in a cottage in the country of Anglesey, standing by itself in a marshy flat pastural inland district. Well built. Dry sanitation. Water supply from a shallow open well nearby. Works as labourer.

Case B 1.—Elias H. Was born and has always lived in the same place, a village in Carnarvonshire, situated inland high up on a mountain side. Small terrace house in exposed situation. Well built, dry sanitation and good water from a mountain spring.

Case B 4.—Lloyd J. Lifelong residence on a farm in Denbighshire, situated in an island district on a hillside and on dry rocky ground. The house is large, built of stone and dry. Water supply is unsatisfactory. It is obtained from a well placed under the floor of the kitchen. It is thus liable to be fouled from the farmyard where pigs, cattle and sheep congregate. Works on farm in summer and is a builder's plasterer.

Case B 5.—Nesta R. Born and always lived in a small town in an industrial area near Wrexham. The house is well built of brick and dry. Water supply from mains. Housework, most of time indoors.

Case B 6.—Kathleen S. Born and has lived with her parents on a farm in Denbighshire, situated on a hillside bordering a narrow inland valley. House built of stone and in good repair. Dry sanitation. Water supply from a well. School teacher.

Though the cases selected had a common factor in always having lived in the same place the resemblance ends there. The histories show that the disease may begin in persons living near the sea, in inland mountain valleys, open country districts, towns or industrial areas. The type of house ranged from humble cottage in the country or back street to a large house or villa. Some had spent their lives mostly indoors, others had worked in the open.

The remaining fifty-five cases had moved from one place to another. Points of interest are noted below:—

Case A 16.—Mrs. Lew. Farmer's wife. Present illness began in 1915-16. At that time had been living on a farm in Merionethshire for nine years. Water was from a shallow well in the farmyard and often tasted peculiar. The present occupants who were interviewed state that the water has often a fatty scum and that the dead bodies of rats have been noticed in the well which is not properly covered. The well is close to the house in the farmyard and is almost certainly contaminated from the yard and a nearby duck pond.

Case A 23.—Mrs. Pl. A few months before onset of present illness came to work as governess in village in Northamptonshire. The water supply was bad. Her employers and the other servants drank bottled aerated water or boiled the local supply. She was careless and often drank the water and noticed that it had a brackish taste. The water came in pipes from an open stagnant pool or small reservoir nearby. These statements were not confirmed.

Case A 27.—Mrs. Rob. Lived in London till three years before onset present illness, when married and moved to a village in Denbighshire. The sanitation was faulty, the terrace in which she lived being drained by a cesspool placed in the back garden. This overflowed and fouled the land and was later closed by order of the M.O.H. Confirmed.

Case B 9.—Mrs. Wil. Has lived at present address for twenty years. Small cottage in coastal village in Anglesey. The walls are damp and water collects on the floor. Water from a public well of old-fashioned type in village.

The only recurring feature in these cases seems to have been an unsatisfactory water supply, generally obtained from wells which were liable to pollution. In thirty-five control cases (Classes *D* and *E*) details of the water supply were also noted. Water was obtained from a main supply by pipes in twenty-three and from private wells in eleven. It is an interesting fact, when taken into consideration with the above, that in only one case (*E*. 32, Mrs. Rob.) was the water supply stated to be unsatisfactory.

Summary and Comments.

(1) No instance was noted of two or more cases having lived together in the same house, town or district. Such examples are probably rare. The rule is to find cases scattered over a wide area, one in this village, another in that town, and so on.

(2) Contact with rats and tick-bites were found in some cases but not with any special frequency when compared with the control cases of other diseases of the nervous system.

(3) The majority of cases had moved about from place to place. Ten were found, however, who had lived in the same house or district most, if not all, of their lives. In these the environment and habits were noted. In the remainder a search was made for common circumstances. The only recurring feature was an unsatisfactory water supply. In most cases this was derived from a well, which was in such a position as to be subject to animal pollution.

SYNOPSIS.

The main object of this work was to note the frequency and distribution of disseminated sclerosis in North Wales, and to inquire into the occupations and living conditions of affected persons. At the same time it was found convenient to study the subjects of age, sex, injury, exposure, pregnancy and heredity. The conclusions reached are in accord with what is already known concerning these events in their relation to the onset of the disease.

The method adopted, of working through the doctors in practice in the district, was most satisfactory. The total number of cases, however, was too small to be of much value in forming direct conclusions. This difficulty was partly overcome by comparing them with a series of control cases of other diseases of the nervous system, taken from the same area and similarly investigated. Diagnosis presented another difficulty as post-mortem evidence was lacking. Of the total 65 cases, 39 were typical clinical examples, 10 were early cases in which disseminated sclerosis was the probable diagnosis and 16 had died of the disease, notes being obtained from the doctor or hospital records. Doubtful cases were excluded and placed among the controls. The patients were visited at their homes and the information obtained about their living conditions checked by the local doctor.

Some 65 cases were found in an area having a population of 492,049. This gave a rate of 1 per 8,600 inhabitants. They were scattered over the province along the lines of densest population. Anglesey, however, appeared to have more than its share, but not much more. Dark-complexioned types predominated (a local feature) and thin and tall persons were met with more frequently than short and stout individuals.

The distribution between urban and rural districts was about half and half, a proportion closely resembling that of the general population. In the matter of occupation, domestic and agricultural workers predominated to about the same extent in both disseminated sclerosis and the control cases. The proportion in each was about the same as that found in the general population.

The mode of life and habits were noted in the hope that some common circumstance might be detected. No instance was found of two or more cases having lived in the same house, street or district. The only recurring feature was an unsatisfactory water supply, in many cases derived from a well liable to pollution.

The results which have been recorded are therefore for the most part negative. The disease was found to be a relatively common one in North Wales, ranking in frequency however after encephalitis lethargica and its after-effects. Almost all the chief occupations were represented but the farming classes did not appear to be more likely to develop disseminated sclerosis than other diseases of the nervous system. There was no frequency among woodworkers. Evidence was also lacking to support the view that the rural incidence was greater than the urban. It is possible that had these cases been seen at a city hospital they would, coming from North Wales, have been placed in the "Country" class, whereas in reality about half of them were living in small towns.

It is open to question what importance, if any, may be attached to the finding, in some cases, of an unsatisfactory water supply. If the disease is infective in origin and this comes through the water, surely one might expect to find instances of more than one case infected from the same supply. It should also be remembered that the inhabitants of outlying or country districts depend largely for their water supply on wells, and even in the small towns the water supply may not be up to the standard of purity of that supplied to larger towns and cities. Judging from the impressions of others, disseminated sclerosis appears to be notably frequent in remote districts such as the West of Scotland and the North of Ireland. It may be that this frequency is related more to an impure water supply than any natural features of the district or pecularity of occupations. This view is offered in no sense as a conclusion but rather as a suggestion arising out of the experience of the present work.

In conclusion the writer acknowledges with gratitude the help he has received from the medical practitioners of North Wales, who made the work possible by their ready co-operation and interest. He is indebted to the Medical Research Council for a grant to cover expenses and to Dr. E. I. Spriggs, Senior Physician at Ruthin Castle, for much valuable help and advice in the preparation of this account. He is grateful to Dr. Bradwen Hughes of the Penrhyn Hospital who enabled him to consult the case notes of the late Dr. John Owen of Liverpool, by whom many of the cases had been formerly seen. Thanks are also due to Dr. Henry Cohen of Liverpool for information relating to certain cases which had been in Liverpool.

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CENTRAL MECHANISM OF THE REFLEX ARC.

A Description of a Ballistic Model in Terms of which to Unify Explanations of Spinal Reflex Activity and Certain Changes in the Voluntary Electromyogram in Man.

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In a recent paper (*Brain*, 1930, liii, 344) it was shown that the changes which take place in the voluntary electromyogram as a result of fatigue could be explained in terms of a mechanism having certain specified properties somewhere on the motor side of the reflex arc central to the lower motor neurones. Since this mechanism must participate in all the activities of this reflex arc which lead to a motor discharge, it must be determined how far the properties here ascribed to it would influence its behaviour in local reflex activity.

In 1925 Sherrington (*Proc. Roy. Soc. Lond.*, B. 1926, xcvii, 519) put forward a scheme of reflex excitation and inhibition based upon the activities of a functional unit in just this situation.

Sherrington points out that the current conception of the neuronic mechanism underlying the conduction of the nervous impulse contains certain elements which may be shared by the interneuronic mechanism responsible for its intercellular transmission. "In the Nernst theory developed by Lapicque, Hill, and others, the rise in concentration of ions for effective excitation must be in amount and rate above a certain critical value. And the theory takes account of a process, inherent in the conditions attending the establishment of the local ion-concentration, which tends to take those ions out of the sphere of action, a process for which diffusion and adsorption have been assigned as probable causes. This process, when the production of further excitation-ions ceases, removes the local concentration, the excitation ceasing" (p. 520).

This conception of the production locally of some substance (ions) whose presence determines nerve-fibre excitation and conduction has been extended by Sherrington to explain the transmission of central excitation. For this, the existence of a mechanism providing an "exciting state or agent, E," is postulated. In the same way an "inhibitory state or agent, I," is provided to mediate the transmission of central inhibition. The properties of this mechanism are defined by the following characteristics of E and I.

With regard to E, "The notion meant to be conveyed is not that of a continuous level of intensity of E, persisting, e.g., at C, after a single-shock stimulus or during a tetanic one. It is that in response to a single centripetal impulse there results, to use a term already suggested, a 'charge' of E, which shoots up to a certain amount (intensity) and then, less rapidly, declines" (p. 522). "The production of E, though a discontinuous process, can by repetition, especially of frequent and of strong centripetal impulses, lead to a continuous supraliminal residuum of E, above which runs a fluctuating intensity with fluctuations corresponding in rate of frequence with the frequence of the external stimulus" (p. 523). C is the "central organ" or mechanism above referred to, and it "must of course lie down-stream from the afferent terminals themselves" (p. 524), in "a structure which is something other than a nerve fibre" (p. 521). In the central field "extending between the terminals of the fibres of the afferent nerve and the emergent motor axon toward which they conduct, there are probably various other such loci, some at successive levels" (p. 524).

With regard to I: It stands for "a state or agent which produces lessening or total disappearance of E" (p. 528). "The Nernst theory of excitation, and the development of it by Lapicque, Hill, and others, recognize the existence of a process counter to the local accumulating of excitatory ion-concentration" (p. 528), and the effect of I "may be essentially an active acceleration of the spontaneous dissipation of an exciting agent or state, e.g., an acceleration and augmentation of that deconcentration process already taken account of in the Nernst theory of excitation" (p. 529). But I "not only accelerates the disappearance of a state of excitation, it also carries the condition of the excitable structure to a state farther removed from excitation than is its normal resting one" (p. 529). "The state or agent immediately responsible for the central inhibition does not draw its source directly from a co-existent state of excitation. It does not arise from something furnished by the state of excitation or by the exciting agent" (p. 530). But though "it is assumed that the I state or agent can be produced independently of E, just as it is universally accepted that excitation can arise and exist independently of I, that assumption regarding I does not indicate that excitation has no relation to or consequences for the production of I, and *vice versâ*" (p. 531). It is implied with regard to I "that like E its quantity or concentration after cessation of the stimulus of the inhibitory afferent, automatically subsides or deconcentrates, and that its amount or concentration and its persistence exhibit various degrees, one factor in them being production or presence of E, which tends to neutralize it" (p. 531).

Although this centre is assumed to act by the production of two different, mutually antagonistic substances, E and I, units of which are liberated by an exciting and an inhibitory impulse respectively, the time relations of production and disappearance of each are closely alike. Observations of Beritoff and Adrian are quoted (p. 531) in support of the probability of their being, unit for unit, contrasting equivalents. This seems to be true not only of the interaction of minimal units of either, but, further, with stronger stimuli "the central inhibition-state, like the central excitatory, lasts longer, its persistence being evidenced by after-action analogous with the 'after-discharge' from persistence of E" (p. 532). Since with quiescence of the arc neither of these agents is present, the production of E and of I resembles the shifting of some central balance in directly opposed senses. "The condition of the material of the common locus seems altered in two diametrically opposite ways by the two antagonistic arcs" (p. 533).

To summarize the characteristic particulars of the system which Sherrington has postulated, we find that in the first place it lies up-stream or central to the lower motor neurone, i.e., in the position which the mechanism assumed to exist, from a consideration of the effort syndrome, must occupy.

It is normally in a condition of stable equilibrium corresponding to quiescence of the reflex arc. From this condition it is capable of being disturbed in two diametrically opposed directions—one corresponding to excitation and the other to inhibition. When so disturbed it tends of itself to return to the pre-existing condition of neutrality or equilibrium. A single exciting impulse tends to displace it to a certain degree in one direction—a single inhibitory impulse tends to displace it an exactly equal degree in the other direction. Stronger exciting influences, i.e., more exciting impulses, and stronger inhibitory influences, i.e., more inhibitory impulses, will tend to displace it to a corresponding greater degree in these two respective directions.

This tendency toward displacement is not a continuous one maintained in any way by the impulses responsible. The effect of each impulse is rather that of "impact" than of a continuous force, resulting in a disturbance which "shoots up to a certain amount (intensity) and then, less rapidly, declines" (p. 522).

Taken together these characteristics are strikingly similar in all respects to those of the elasticity of a simple ballistic system.

But one qualification is necessary if the parallel is to be an accurate one, and here the time relations are all important. An inertialess elastic system disturbed by impact, however small, from its position of equilibrium would shoot off to infinity at once. The addition of some property akin to lag or inertia, some quality like mass, imposes a limit to the resulting disturbance and makes it proportionate to the impact. It determines the time relations both of the disturbance and of the recovery phase. Further, it provides that overshooting of the position of equilibrium which is the basis of the oscillations and which in the system under consideration here is shown as "rebound." The fact that not only is the degree of disturbance the same for antagonistically equivalent units of excitation and inhibition, but that the time relations of the disturbances also are identical, provides a very strong inducement for regarding them as oppositely directed processes acting upon a single mechanism, and for regarding the mechanism held to be responsible for the effort syndrome as capable of accounting for these other properties of the reflex arc.

Let it be assumed that immediately central to the final common path there exists a mechanism through which, and through which alone, the neurones constituting that final common path may be excited. These neurones themselves are capable only of being either excited or not excited; the central mechanism is capable of a further condition referred to as being inhibited. The mechanism has properties akin to damped elasticity and to mass or inertia. It may have other properties in addition, but these two are necessary and may prove sufficient. Excitation entails the disturbance of the equilibrium maintained under the elastic process within the system. One unit of excitation acts upon this system as an impact displacing it from its position of equilibrium in one direction. Two units of excitation will act as an impact of double the size, and so on. Units of inhibition act as impacts upon the system of exactly the same size but in the reverse direction. These impacts may be delivered in whatever condition of rest or disturbance the system may be. The system is symmetrical about its position of equilibrium so that it will be displaced to an equal amount in the two opposite directions by an equal number of excitation and inhibition units respectively. The factor which determines excitation of the final common path or motor neurones is the degree of displacement—the greater the degree of displacement the greater the number of neurones excited—the rate of displacement having no effect upon their excitation.

Let us now take the experimental facts which Sherrington has already brought under examination, considering first those in respect of excitation alone.

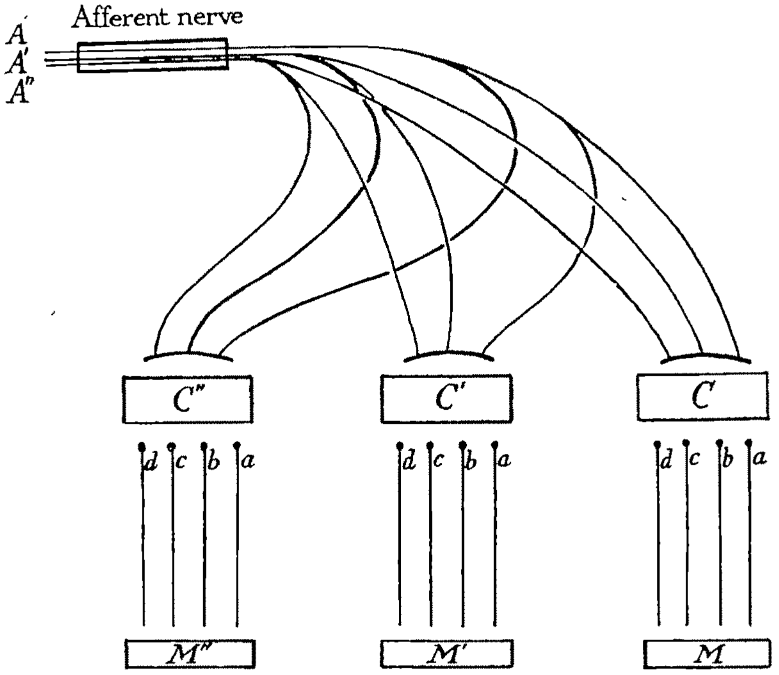

FIG. 1.—Let A A′ A″ represent fibres of a purely excitatory afferent nerve. Let each of these fibres be connected with all of the central organs, C C′ C″. Let stimulation of A A′ A″ produce changes in C C′ C″ which result in excitation of one or more of the motor neurones M *a b c d*, M′ *a b c d*, M″ *a b c d*, leading to contraction of corresponding elements in the muscle units M M′ M″

(1) "With increase, within limits, of strength of a single-shock stimulus applied to the afferent nerve there occurs increase of the muscular response" (p. 525).

A stimulus of small strength will excite few nerve-fibres and provide few excitatory impacts; the system will be disturbed by a certain amount. A stimulus of greater strength will provide more excitatory impacts and disturb the system by a greater amount. But if X impacts displace the system through a distance or to an amount D, 2X impacts will displace it less than 2D, because as the displacement increases the force tending to restore the system to its position of equilibrium also increases. There will therefore be a limit to the effective increase in displacement, and therefore to the number of motor neurones excited with increase of the stimulus, quite apart from any consideration as to the number of neurones available for excitation. Hence, not only will

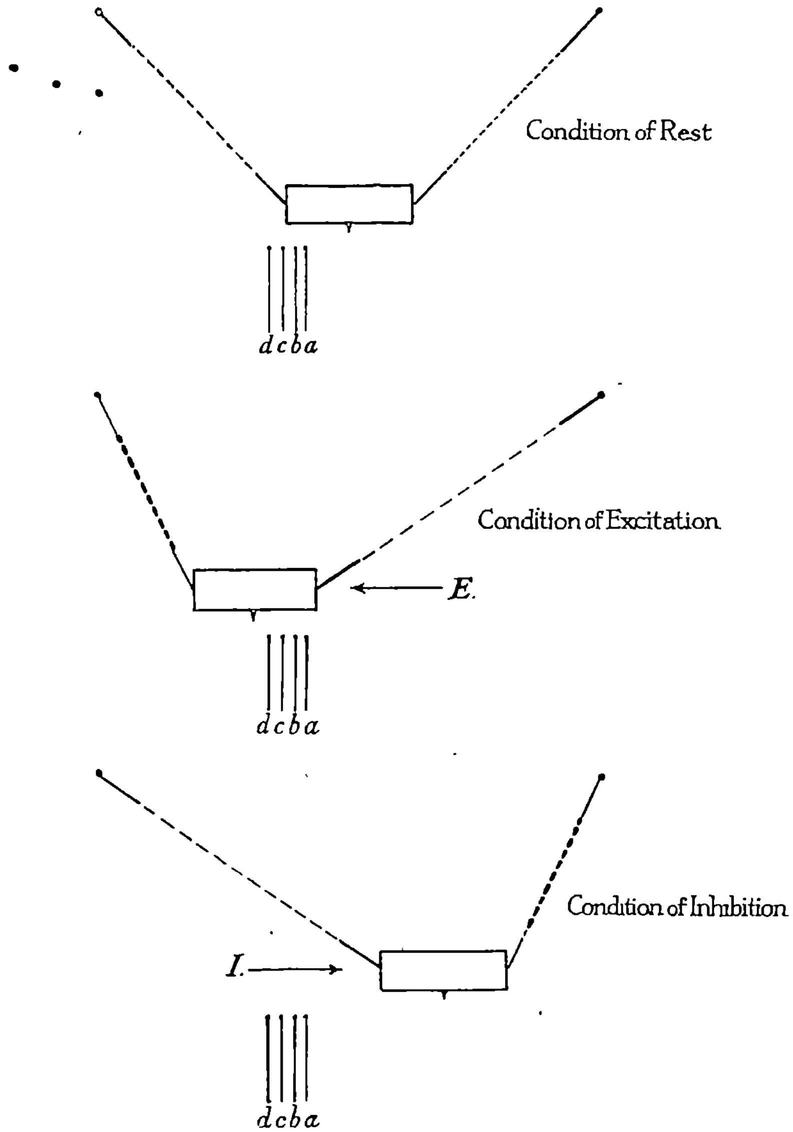

Fig. 2.—The ballistic model of the central organ, C.

there be grading of the efferent discharge and of the consequent motor response in accordance with grading of the single shock stimulus of the afferent nerve, but this grading will not be strictly proportionate, the increase in response will fall off progressively more and more rapidly as the stimulus strength is increased, and will sooner or later reach a limit beyond which no further increase will follow from increasing the stimulus.

(2) "The single-shock reflex exhibits after-discharge. With increase, within limits, of the strength of a single-shock stimulus of the afferent nerve, the reflex after-discharge is increased and prolonged."

A single stimulus providing along different afferent fibres one or more excitation units of impact will displace the system to a proportional degree in the direction of excitation. The inertia of the system provides a lag in the return to equilibrium which determines that the displacement shall outlast the stimulus for a period which will depend upon the relation between the inertia and the restoring force or elasticity. With increase of the stimulus there will be increase of the number of excitation impacts, increase in the amount of displacement and increase in the after-duration of sufficient displacement necessary to determine continuation of the motor discharge. Since there will be not only an increase in the duration of sufficient displacement to excite the motor units of low threshold, but also, the displacement being greater in the case of the stronger stimulus, an increase in the number of motor units affected, the after-discharge will be both prolonged and increased. However, just as the process discussed under (1) reaches a limit, so here also the same factors determine the limit to which this proportionate increase can be pushed by increase of the stimulus strength.

(3) "In many excitatory reflexes mere prolongation of the otherwise unaltered stimulation of the afferent nerve increases the reflex contraction" (p. 526).

After the delivery of a single excitation stimulus the system returns towards its position of neutrality or equilibrium. The degree of restoration attained at any given moment after the displacing impact is a function of the time interval. A second impact delivered before complete restoration of equilibrium will reach the system in a phase of partial recovery or partial displacement and, acting from this point, will produce a greater degree of excitation displacement than it would have done had it acted upon the system in the position of equilibrium. The smaller the interval between the delivery of the two stimuli the smaller will be the amount of recovery achieved, i.e., the greater will be the actual displacement when the second arrives, and the greater will be the final amount of displacement provided by both stimuli in succession. Prolongation of the otherwise unaltered stimulation of the afferent nerves, by providing a succession of afferent impulses and a succession of excitation impacts, will thus cause a gradually increasing degree of displacement which will increase the number of motor neurones affected and hence also the reflex contraction. This process has been given the name "recruitment" by Sherrington.

It will be noticed that since the restoring force increases with the amount of displacement, with a given stimulus (i.e., with a given number of simultaneous excitation impacts per stimulus), a degree of disturbance will sooner or later be reached at which, under the increased restoring force, the amount of recovery which has taken place after each stimulus will become equal to the amount of disturbance which the subsequent stimulus is capable of providing at that degree of displacement. After this point is reached further prolongation of the stimulus will produce no further maximal displacement, so that "the recruitment obtainable by prolonging a given stimulus of the afferent nerve does not, if that stimulus be below a certain intensity, proceed so far as to enlist all the motor-units of the whole motor-unit aggregate, however long the duration may be extended" (p. 526).

This successive summation of effects will clearly account also for the fact that "mere prolongation, e.g., by repetition, of a brief external stimulus of the afferent nerve has usually the effect that a stimulus, which when brief is subliminal, becomes by prolongation, e.g., repetition, liminal or supraliminal" (p. 521). Sherrington has shown that this result is explicable upon the basis of some central structure which "has, unlike nerve-fibre, no absolute refractory phase, and has, as have many other cell-structures, including skeletal muscle-fibre itself, a property of summating its successive reactions when these are not too far apart in time" (p. 521). Again, with a slow rate of repetition the inter-stimulus recovery will be greater in amount than with a high frequency of repetition. Therefore, rapidity of stimulation will provide not only a greater mean value of continued displacement but also smaller degrees of variation in this displacement, so that "the individual fluctuations will be smaller, and the mean intensity higher, in proportion, other conditions equal, as the frequence of the stimulus is rapid". (p. 523).

(4) "'After-discharge' contraction will exhibit no rhythm corresponding, as does that of the stimulation contraction period, with that of the external stimulus" (p. 523).

From the considerations detailed in (3) it is clear that the fluctuations in the motor discharge during a series of stimuli in slow succession to an excitatory afferent nerve will be in step with the stimuli themselves—the rhythm of stimulation and the rhythm of discharge will be identical. When the series is interrupted there will be some after-discharge (see (2)), but this after-discharge will be subject to no fluctuations and will therefore exhibit no rhythm corresponding, as does that of the stimulation contraction-period, with that of the external stimulus.

(5) "Increase of strength (within limits) of the stimulus applied to the afferent nerve shortens the initial latent interval of the reflex" (p. 526).

Increase of the strength of the stimulus provides an increase in the number of simultaneous excitation-impacts, an increase in the rate at which the inertia of the system is overcome and a decrease in the time necessary for the attainment of any particular degree of displacement. This will entail a shortening of the initial latent interval of the reflex.

(6) "Increase, within limits, of strength of stimulation of the afferent nerve increases the muscular response, not only when the stimulus is a single shock, but also when it is tetanic" (p. 527).

Clearly the change from increase of a single shock stimulus to increase of strength of a tetanic series provides an increase not only of the number of simultaneous excitation impacts derived from a single stimulus but also an increase in the number of the simultaneous impacts occurring at each repetition of the stimulus when this is tetanic. Therefore increase of the strength of tetanic stimulation will, by increasing the amount of additional displacement per stimulus, increase also the mean value of the maintained displacement and hence the average number of motor neurones involved and through them the muscular response. This increase will be subject to the same limiting factors as have been discussed under (1).

(7) "Persistence of after-discharge, both under single-shock and tetanic stimuli, attaches in one and the same reflex-sample very unequally to different individuals of the 'motor-unit' group engaged" (p. 527).

The delay in the recovery process, which is the result of the inertia of the system, determines the after-discharge. Since recovery is progressive those motor neurones which require for their excitation greater amounts of displacement will be provided with this necessary condition for a shorter period following the cessation of any given stimulation than will the motor neurones which require smaller amounts of displacement. Further, with variations in the strength and effective value (repetition-rate, prepotency, &c.) of the stimulus persistent high degrees of displacement will be less frequently met with than will persistent low degrees of displacement, so that the former motor neurones will be affected not only to a less degree in each case, but also less often in all cases than will the latter.

These facts and explanations are concerned with disturbance of the system in one direction only, i.e., that of excitation. It must now be considered how far the same properties will provide an explanation for the effects of inhibiting stimulation.

(8) "Increase, within limits, of the strength of the stimulus of the inhibitory afferent increases the amount of relaxation which the inhibitory reflex can produce in the contraction of a given excitatory reflex" (p. 534).

Increase of the strength of the stimulus provides a greater number of inhibitory impacts and will tend to produce a greater amount of displacement in the direction of inhibition. This, summing algebraically with the pre-existing excitatory displacement, will diminish this excitatory displacement to a greater degree, produce an increase in the number of motor neurones released from activation, and increase the amount of relaxation in the muscle response.

As the strength of the stimulus producing inhibition is progressively increased a stage will be reached at which the excitatory displacement is reduced wholly to zero, when total relaxation will occur and there will remain no after-discharge. With further increase in the strength of the stimulus the reduction in the excitatory displacement increases still further, so that this becomes negative in amount, i.e., residual inhibitory displacement is left which is gradually reduced to zero by the elastic restoring forces of the system. The delay in this restoration of equilibrium provides the "inhibitory after-action." This explains why it is that against a given excitatory reflex "the weak stimulus of the pure inhibitory afferent produces a lesser immediate 'partial' relaxation of contraction and less curtailment of after-discharge contraction than does the moderate stimulus, while the strong stimulus causes immediate 'total' relaxation, precludes after-discharge contraction altogether, and leaves in regard to some of the motor neurones an inhibitory after-action" (p. 535).

(9) "The central action evoked by the same stimulus of the inhibitory afferent which causes only small relaxation of the contraction excited by a strong stimulus of the excitatory afferent can cause large relaxation

of the contraction excited by a weak stimulus of the excitatory afferent" (p. 536).

A given stimulus of an inhibitory afferent provides a certain number of inhibition impacts. The effect of these summates algebraically with a large excitation displacement in the case of the strong stimulus to the excitatory afferent and with a small excitation displacement in the case of the weak stimulus. In the former case the displacement will be reduced to a smaller degree, the number of motor neurones thrown out of activation will be diminished and the relaxation will be less.

(10) "Experiment shows that, within limits, mere prolongation or repetition of the otherwise unaltered stimulus applied to the inhibitory afferent increases the amount of inhibitory relaxation of a given reflex contraction" (p. 536).

It is unnecessary to elaborate in appropriate detail the way in which this result can be as readily explained. This inhibitory recruitment can be explained on a basis exactly similar to that outlined in explaining excitatory recruitment (§ 3).

(11) "Within limits, increase of strength of the inhibitory afferent's stimulus gives increase of the amount of relaxation of a sampled excitatory reflex" (p. 537).

Clearly the increase in relaxation effect shown to be explicable for single inhibitory-afferent stimuli may be also shown to be explicable for tetanic stimuli—just as the excitation response was shown to increase with increase of both single-shock and tetanic stimuli to an excitatory afferent.

(12) "An intercurrent stimulation of the inhibitory afferent applied in the course of an excitatory reflex can, besides producing relaxation partial or complete of the reflex contraction, be followed after withdrawal of the inhibitory stimulus by temporary impairment of the restoration of the contraction under continued unaltered application of the excitatory stimulus, the returning contraction exhibiting slower development than did the corresponding part of the original contraction at initiation of the excitatory reflex before occurrence of the inhibition. Also the impairment of return after a given inhibitory stimulus is greater as against a weaker excitatory stimulus than as against a stronger" (p. 537).

Each stimulus to an inhibitory afferent nerve provides a certain number of inhibition impacts which diminish the excitation displacement by a proportionate amount. With continuation of the excitatory stimulation the full pre-existent excitation displacement is restored.

But immediately following the delivery of the inhibition impacts the system will be moving towards the position of equilibrium. Therefore before the excitation displacement can be restored the whole system must be retarded in its equilibrium-recovery phase, arrested and set again into motion in the direction of excitation. By virtue of its inherent inertia these processes will require a definite time for their occurrence in sequence; also a given number of excitation impacts will produce less further shift in the direction of excitation when the system has momentum in the reverse direction than when the system has none. For these reasons the time taken to increase the excitation displacement from the amount present at the cessation of inhibition to the full amount present before inhibition, will be greater than that originally occupied by the same amount of increase at the initiation of the excitatory reflex before the occurrence of inhibition. Also since momentum in the direction of inhibition is constant for a given inhibitory stimulus, it will delay excitation recovery to a greater extent when the excitation impacts are few than when they are many, i.e., the impairment of return will be greater when the excitation stimuli are weaker than when they are stronger.

(13) "A stimulus of the inhibitory afferent counteracts the effect of the stimulus of the excitatory afferent more in regard to the motor-units of higher threshold for the excitatory afferent than in regard to those of lower threshold for that afferent, and does so both in respect to the stimulation period of the excitatory afferent and to the after-discharge period" (p. 538).

A given inhibitory stimulus will only affect a proportionate amount of shift in the direction of inhibition, i.e., only diminish the excitation displacement by a certain amount. The motor neurones which require for their activation greater amounts of excitation displacement will not only find this reduced below threshold value as a result of various inhibitory stimuli more frequently, but they will be deprived of the requisite amount of excitation displacement earlier, and have it restored later, than those which require smaller amounts of displacement. Moreover, the inhibitory impacts, which accelerate the equilibrium restoration tendency having play after cessation of excitatory stimulation will, by hastening this restoration, diminish the after-discharge. Since also the greater degree of excitation displacement necessary to activate the motor neurones of higher threshold will be less rarely left over, and certainly left over for a shorter period, than that required for the motor neurones of lower threshold, the former will suffer greater eclipse from inhibition than will the latter, in respect also of the after-discharge period.

(14) "With a given excitatory reflex a stimulus of the inhibitory afferent can more readily relax the after-discharge contraction than cause relaxation of the contraction during the actual course of the excitatory nerve-stimulation" (p. 538).

Since during the after-discharge period the system is already moving in the direction of excitation displacement reduction, i.e., of inhibition displacement increase, a stimulus of the inhibitory afferent will produce more rapid and more extensive change in the direction of inhibition than it will when its inhibition impacts impinge upon the system during maintained excitation displacement. Therefore it follows that it will more readily affect the after-discharge contraction than the contraction during the course of excitatory nerve stimulation.

(15) "The later in the course of the after-discharge the inhibitory stimulus be applied the less strong need that stimulus be in order to cause relaxation of the after-contraction" (p. 538).

The later in the course of after-discharge the inhibitory stimulus is applied the greater will be the velocity of the system in the direction of inhibition and the fewer the number of inhibition impacts (the less the strength of the stimulus) required to diminish the existing excitation displacement by an amount which will reduce it below the value required by the motor neurones for their activation.

(16) "The after-discharge contraction does not tend to return after an intercurrent inhibition has interrupted it" (p. 538).

Since the system is already travelling in the direction of inhibition when the inhibitory impacts arrive, in the absence either of further excitatory stimuli or of inhibition rebound due to the momentum of the system on its return from any very considerable inhibition displacement (if this results), there can be no tendency for any further movement in the direction of excitation, i.e., no further tendency for the return of after-discharge.

(17) "The latency of the reflex inhibition is less with stronger stimuli, single-shock or tetanic, of the inhibitory afferent than with weaker, and correspondingly recruitment of inhibition proceeds more quickly under stronger tetanic stimuli of that afferent than under weaker" (p. 538).

These results are fully explicable as determined by the inertia of the system. The argument is precisely similar to that detailed in Sections (5) and (6) for the latency and recruitment of excitation effects and need not be repeated in respect of inhibition effects.

(18) "Inhibitory 'eclipse' of the after-contraction occurs, and takes place earlier, other conditions equal, the stronger the stimulus of the inhibitory afferent" (p. 539).

The stronger the stimulus to the inhibitory afferent the earlier will the excitation displacement be reduced below threshold value and the greater will be the likelihood of its total reduction upon cessation of excitatory stimulation.

Sherrington has drawn attention to the long latency with which the after-discharge-reduction effect may follow application of the inhibitory stimulus. He finds that this can be illustrated by means of his scheme and diagram if "it be supposed that owing to the circumstances, e.g., state of the central organ, the value of E be throughout greater than was actually allowed to it." We have seen that a limit beyond which increase of the excitatory stimulus leads to no further increase of the response is imposed by the increase of the elastic restoring force with increase of the displacement. Clearly another factor determining a similar limit is also present, i.e., maximum number of motor neurones which can be activated by the mechanism. It is improbable that any considerable proportion of the motor neurones require degrees of excitation displacement which approach the maximum attainable. It is much more likely, since it is a system which is characterized by changes accompanied by momentum, that it is capable of excitation-displacement to a degree which lies considerably beyond that which is required for activation of all the motor neurones innervated from it. That this is so follows also from the fact that upon cessation of a reflex contraction the after-discharge contraction commonly persists at the same level as the concurrent excitation contraction, and only later falls gradually away. This would follow if the level of displacement maintained by the constant excitatory stimulation is considerably greater than that required by the threshold of the motor units activated. Although the recovery begins immediately the excitatory stimulus ceases, there will be the more delay before the displacement has been reduced to the above threshold level, the higher the maintained excitation displacement level, and throughout the period of this delay the after-discharge contraction will be unaffected.

Further, an inhibitory stimulus applied during the course of excitatory stimulation may not suffice to reduce the existing excitation displacement below the threshold value of any of its activated neurones. Yet it certainly will effect some reduction: a reduction which will show itself by diminution of the after-discharge. The smaller amount of displacement will, after cessation of the excitatory stimulation, take less time for further reduction to below threshold level than would have been required for the original amounts of displacement prior to the delivery of the inhibitory stimulus. "Therefore the after-discharge contraction, although it may still be a long-persisting one, will yet not be so prolonged as when no intercurrent inhibitory stimulus is given, although that stimulus as judged by absence of immediate outward (relaxatory) result be a seemingly ineffective one" (p. 539).

We have seen previously, Sections (5) and (6), that the increase of the restoring force with increase of displacement makes it more difficult for a given number of excitation impacts to increase the displacement when this is already considerable than when it is small. It follows also that tetanic stimulation must be continued for a long period to restore a given amount of excitation displacement, when the original level of this is high, than when it is low. Therefore a slight inhibitory stimulus which may achieve a considerable reduction of excitation displacement from a high level (Section 12) may in this way very much delay the return to the original level of displacement which follows its cessation, and considerably curtail the after-discharge after a very long latency.

(19) "An inhibitory stimulus delivered during the stimulation period of the excitatory reflex may fail to cause at delivery any relaxation of the reflex contraction, and yet produce in the 'after-discharge period' an eclipse of contraction which is 'total,' i.e., affects all the motor neurones engaged in the excitatory reflex, thus showing that though seemingly effectual on none of those motor neurones at the time of its occurrence, it yet affected all of them" (p. 540).

An inhibitory stimulus whose strength is sufficiently well adjusted in relation to concurrent excitation, may reduce the amount of excitation displacement down to, but not below, the threshold level for any of the neurones involved. It will thus not produce any relaxation of the reflex contraction. There may, however, be comparatively so very little extra excitation displacement left that upon cessation of the excitatory stimulus the motor neurone activities fall off at once and the eclipse of the after-discharge is "total."

(20) "The inhibitory after-action persists longer after cessation of a stronger than after cessation of a weaker stimulus of the inhibitory afferent, other conditions equal" (p. 539).

Since the inhibition impacts supplied by the stronger inhibitory stimulus will result in a displacement of the system further in the direction of inhibition than will result from the weaker inhibitory stimulus, the delay in recovery from inhibition will be longer in the former case. It readily follows also from this that "the latency of a post-current excitatory reflex of given strength is longer, other conditions equal, the stronger the precurrent inhibitory reflex, and the closer the stimulus of the excitatory afferent follows on cessation of the stimulus of the inhibitory afferent" (p. 539).

(21) "A precurrent stimulation of the inhibitory afferent, even, though showing no effect on the resting muscle, may prevent entirely, or retard and diminish, the contraction response of a following stimulation of the excitatory afferent" (p. 541).

In the system here defined a given inhibitory stimulus would be expected invariably to result in the same amount of change within the system. The way in which this change would influence the motor neurones which it has the power of activating would depend entirely upon the degree of displacement and the momentum of the system at the moment at which the given inhibitory impacts arrive. Similarly, a given excitatory impulse will have invariably the same effect upon the system producing momentum in the direction of excitation displacement or reducing momentum in the direction of inhibition displacement.

Thus a precurrent stimulation of an inhibitory afferent will give the system a momentum in the direction of inhibition. A following stimulation of the excitatory afferent will produce momentum in the reverse direction which may be completely used up in overcoming the inhibition momentum (in which case no displacement in the direction of excitation will occur, no motor neurones will be excited and no contraction response will follow), or which will be used up in a greater or less degree, determined by the relative values of the two momenta, and the time interval between the moments of delivery of the two stimuli. In the second case the production of displacement in the direction of excitation will be retarded and diminished in a corresponding degree, the activation of the neurones will be retarded and the number affected diminished, so that the resulting contraction response will suffer a corresponding delay and diminution.

It is clearly not essential for the production of this effect that the inhibitory stimulus should be continued up to the moment of delivery of the excitatory stimulus, [so that "even in instances where the stimulation of the inhibitory afferent is withdrawn prior to the following delivery of a stimulus to the excitatory afferent, that latter stimulus if brief (e.g., a single break-shock), of moderate strength, and quite closely ensuent after cessation of the inhibitory stimulus, will not cause contraction" (p. 541).

The strength of any stimulus, inhibitory or excitatory, has been defined here merely in terms of the number of inhibition or excitation impacts repeatedly delivered upon the system in question, and not in terms of the conditions (i.e., current strength and site) of stimulation.

A given inhibitory stimulus may impart to the system much more momentum in the direction of inhibition than is contributed in the reverse direction by an excitatory stimulus similarly delivered but to a different nerve. Such a stimulus will not only produce a much greater amount of displacement but will produce a given amount of displacement in a much shorter time. Therefore the system provides for the circumstances in which a reflex contraction is precluded from following as the result of an excitation stimulus, by a subsequently delivered inhibitory stimulus, provided that this falls in the earlier course of the latent period for the excitatory reflex.

From these considerations it appears that the postulation of a mechanism such as has been described having the properties of mass, which endows it with inertia and momentum, and of elasticity, provides a simple explanation for the observed facts of both excitation and inhibition within the reflex arc.

"Conduction along reflex arcs presents in contrast to that along nerve-trunks characters that may be figuratively described as indicating inertia and momentum" (p. 541).

The reflex-inertia is held to account for temporal summation and recruitment; the reflex-momentum for after-discharge and inhibitory after-action. But "the simple analogy cannot be taken closely, because 'reflex inertia' may be practically absent in cases where considerable 'reflex momentum' is present, and *vice versâ*" (p. 542). Since in any known mechanical system inertia and momentum are both functions of the mass, it is difficult to see how they can be expected to vary independently under purely external influences without postulating some intercurrent reversible alteration—such as in the distribution of the mass—within the system itself.

It is here suggested that if the system is regarded as having in addition to mass the property of elasticity this difficulty is overcome and these discrepancies between theory and observation disappear.

It has been shown above that a system having the properties of mass and elasticity would be expected to behave in a way calculated to give the observed effects as a result of definite excitatory and inhibitory influences. In this scheme the mass of the system contributes the inertia which underlies the phenomena of temporal summation and stimulus—response grading, and that the elasticity provides an adequate basis for the explanation of after-discharge and inhibitory after-action. The occasional lack of parallelism between recruitment and after-discharge is sufficient to lead to hesitation in ascribing them both to manifestations of a single property. There is, however, no reason why different reflex systems having each the same properties should not vary in their possession of different amounts of each—in fact, from a consideration of the much greater facility of certain reflexes it is probable that such differences do occur.

Since we have throughout been inferring the characteristics of the system postulated from the reflex behaviour in which it plays a part, it introduces no further element of complication if we decide that those central systems which underlie reflexes which show exaggerated recruitment and minimal after-discharge have small mass and great elasticity, whereas those which mediate other reflex activities showing minimal recruitment and much after-discharge have much more mass and little elasticity.

SUMMARY.

(1) In a previous paper it was shown that certain changes in the voluntary electromyogram in fatigue and in some pathological conditions probably had their origin within the central nervous system in a specified situation.

(2) The existence of a functional unit in this situation was postulated and the properties of such a mechanism by virtue of which these changes appeared were discussed.

(3) In the present paper a mechanical model is described and its behaviour examined when it is subjected to units of equal and opposite forces.

(4) It has been shown that if by this model be represented the nervous mechanism above postulated, and by the opposing forces the impulses, excitatory and inhibitory respectively, supplied along an afferent nerve, then its behaviour is in every respect in accord with the observed facts of spinal reflex action through the arc in which the nervous mechanism must be located.

(5) From this it is inferred only that the suggested localization of the site of origin of the changes in the voluntary electromyogram is not inconsistent with the observed facts of spinal reflex activity.

CLINICAL AND ANATOMICAL STUDIES ON TWO CATS WITHOUT NEOCORTEX.

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INTRODUCTION.

GOLTZ was the first to keep a dog without forebrain alive for a long period; since then a few other investigators have succeeded in the same experiment. We mention Rothmann, senior, who operated on a dog; Dusser de Barenne, who operated on two cats; Zeliony, on dogs; Dresel and Rothmann, also on dogs; and Karplus and Kreidl, on monkeys. The general conclusion from these experiments is that higher mammals can live without cerebral cortex. They are able to stand and to walk; they have normal muscle tone; they are able to perform isolated movements of the extremities; they keep a normal body temperature, and have a normal rhythm of wakening and sleeping. They show signs of different emotional states such as satisfaction (purring in cats) and anger. They react to sounds, but they appear to be completely idiotic, if such a word may be applied to animals; they do not recognize particular sounds, and do not recognize objects by vision, though the pupillary reflexes are intact. When the rhinencephalon is intact the animals are able to find their food by smell and to eat spontaneously.

The recent clinical interest in the pathology of the basal ganglia suggests new experiments in order to find out whether there is a difference between animals where the cortex only has been removed, and others where both the cortex and the striatum have been removed. In order to contribute to this problem we developed a technique which enabled us to remove one hemisphere of the brain [18] without much danger to the life of the animal. The removal of the second hemisphere, however, proved to be a very difficult task. Out of six animals operated upon, four died within a few days after the second operation from hæmorrhage, infection or "broncho-pneumonia." One "thalamus cat" was kept alive for nine days, and one "striatum cat" survived the second operation until we killed her five months later. The present paper deals with the two animals which survived the second operation for a considerable time.

The technique of the operation differed somewhat from the usual. We worked with local anæsthesia, using a 1 per cent. novocain solution. In order to keep the animal quiet we administered bulbocapnine hydrochloride which produces a kind of "Parkinsonian state" lasting for an hour or two. It was necessary to close the carotid arteries with clamps under ether anæsthesia and to open them about half an hour after the completion of the operation. A description of this technique has been published [18].

The details of the clinical examinations can be seen from the protocols. In the striatal animal we made special examinations, including tests of ocular nystagmus, determination by graphic records of the activity of the animal, and electrical stimulation of the residual brain. These examinations will be summarized in special chapters.

Protocol 1. *Thalamus cat*, "*Mary*."—The *left hemisphere* was removed anterior to the thalamus on July 22, 1926. Immediately after this operation there were torsion spasms to the right side; next day these spasms began to disappear and occurred only during periods in which the general reactivity of the animal was diminished. Between the spasms the animal made circus movements to the left. There were some choreic twitches of the head. Whenever the animal started to walk after a period of rest, the right foreleg developed a tremor. The choreic movements, the torsion spasm to the right and the tremor disappeared soon, and only those symptoms remained which are typical of hemi-decortication, namely hypertonus of the crossed antigravity muscles, a slight paresis and ataxia of the crossed side, and crossed hemianopia. There were the following peculiarities: The animal made very strong circus movements to the left side. It often happened, for instance, that in attempting to eat she missed the food jar four or five times, because she deviated to the left, and was obliged to circle round for another attempt. When the animal was blindfolded, the direction of the circus movements was reversed, the animal now circling to the right. When standing the body always inclined to the left a little. The left pupil and the left palpebral fissure remained narrower than the right.

On October 5, 1926, the *right hemisphere* was removed anterior to the thalamus. There was a definite hydrocephalus of the right ventricle. Five hours later the animal was taken from the operating table. She lay in the left recumbent position and moved the right extremities strongly, the left weakly and elevated her head.

October 6: Vomited during the night. Walks steadily, purrs when petted.

October 8: The animal makes circus movements, usually keeping to one direction for several hours. It does not eat spontaneously; it swallows with excessive movements of the jaws.

October 9: The animal made circus movements to the left (fig. 1). It still dragged the left paws; the left extremities were hypotonic. From time to time the animal changed the direction of its circus movements without recognizable cause. The direction of the circus movements did not change on passive movement of the head. The pupils were very wide and did not react to light.

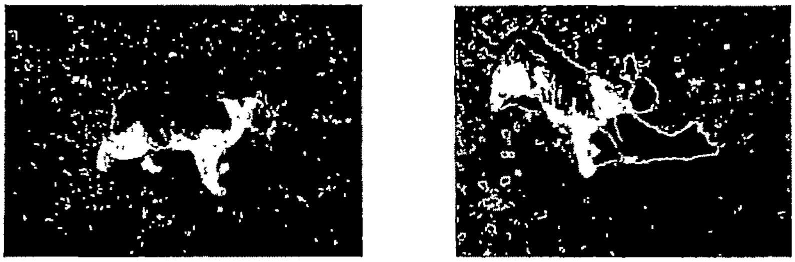

FIG. 1.

October 11: The animal was quieter, but often lay with closed eyes. Usually she circled to the right. When she was fed lying on the left side the right paws developed a clonic tremor.

October 12: The animal was becoming weaker; she stood on extended legs and had tachypnœa.

October 13: Orthopnœa and tachypnœa, the auxiliary respiratory muscles participating; eyes brilliant, no discharge from the nose. The animal looked very dry. Respiration stridorous, expiration difficult. Respiratory rate 120 a minute.

October 14: Found dead.

Necropsy.—The brain was injected with 10 per cent. formalin through the carotids and carefully dissected from the cranium. The contents of the left cranial cavity were covered by a solid membrane of dura, connective tissue and muscle. The right side of the dural sac was filled with a jelly-like bloody exudate. Both lobi piroformes were preserved, but the left was atrophic and discoloured. Only a thin layer of tissue connected the rest of the right thalamus and the olfactory bulb (fig. 2). The left thalamus had been damaged. The brain was hardened in formalin and cut in serial sections.

The serial sections were not available when this paper was written.

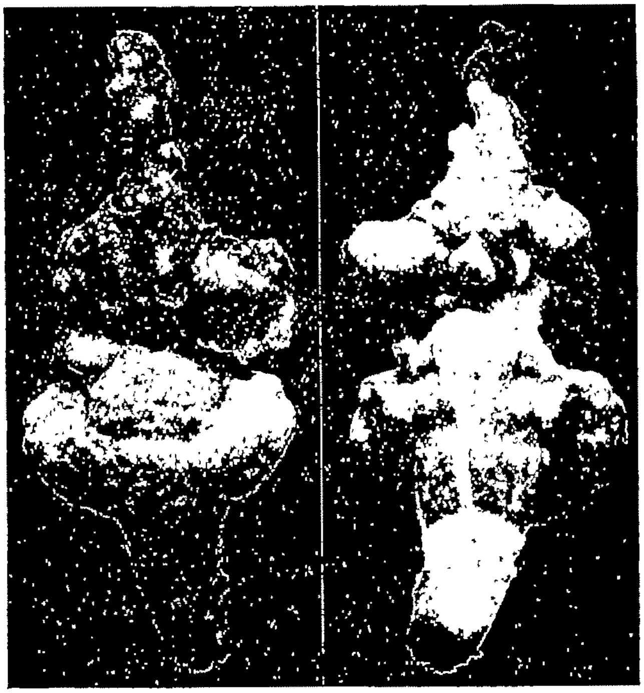

FIG. 2.

Summary.

The "thalamus cat, Mary," was observed for nine days after the second operation. Necropsy shows that the principal aim of the operation had been accomplished. The animal was able to stand and to walk but had a slight paresis of the left extremities after the second operation. States of sleep and of wakefulness could be distinguished. The behaviour of the animal was extremely dull, and it made almost constant circus movements. It changed the direction of the circus movements from time to time without apparent cause.

Protocol 2. *Striatum cat,* "*Kleopatra.*"—August 4, 1926: Removal of the left neopallium. The animal received 0·06 grm. of bulbocapnine hydrochloride and developed marked catalepsy. The carotids were closed with clamps under light ether anæsthesia, and ether was discontinued. The scalp and the left temporal muscles were infiltrated with 1 per cent. novocain solution. The skull was trephined over the left hemisphere and the dura opened. The hemisphere was removed in two parts after the left lateral ventricle was opened by splitting the gyrus fornicatus its entire length. The first part included the cortex with exception of the island of Reil, the second part the island of Reil. The head of the caudate was damaged and probably also a part of the putamen was removed. There was slight hæmorrhage. Two pieces of muscle were left on the base. During the trepanation the left frontal sinus was opened; the hole was closed with wax and a flap of dura was sutured across it. The wound was closed with Michel clips and collodion dressing was applied.

After the operation the animal appeared furious. It lay in the right lateral position and could not rise. When brought into a sitting position it turned its head to the right. The right foreleg was paralysed. The animal followed the examiner with her eyes. The evening after the operation she could not stand, but always fell to the right. Periodically she had wild attacks of running movements with deviation of head and body to the right and mewing.

August 5: The animal was able to stand.

August 7: She had serous discharge from the left nostril. There was definite extensor tone of the right extremities. The animal wandered in circles to the left. The right forepaw was often tilted over. When the animal, after rest, started to walk she developed clonic spasms of both right extremities for a second or so.

August 11: The scar bulged on the left side and fluctuated; the posterior end of the wound was opened and discharged cerebrospinal fluid.

August 19: When the eyes were closed with adhesive strapping the animal tried to remove the adhesive, chiefly with the left forepaw, but sometimes also used the right; then a fine tremor of the right paw developed and its movements were clumsy compared with those of the left. There was still definite hypertonus of the extensors on the right side.

September 11: Animal was in excellent condition. The scars were healed and overgrown with hair. Pupils and palpebral fissures were equal on both sides. She wandered in circles to the left. When lying on her back, head in the symmetrical position, the right hindleg showed definitely more extensor tone than the left. The difference was less pronounced in the forelegs, but the right foreleg was more extended.

The neck-righting reflex was present to both sides, but stronger from the left than from the right. When the animal was held on a basin, head hanging down, the head was in a symmetrical position. On jumping from a chair she landed straight and kept her balance. If blindfolded she inclined to the right and backwards, falling occasionally.

She was quiet and did not move much. Occasionally her head turned to the left and she fell to the left. She tried to remove a blinder with the left forepaw, and in doing so stood on both hindlegs until she fell backwards. She turned to the left (sometimes to the right), sank down and remained there until disturbed. Finally, she fell on her left side and lay there. The shaking movements of the right extremities, which were observed during the first days after the operation, had disappeared. Weight 2·07 kg.

September 27: Until a few days ago the animal had been in excellent condition, but since the 25th it was apathetic, the scar over the left hemisphere was swollen and tender; apparently the animal had an attack of hydrocephalus, and it was decided to operate immediately.

Removal of the right neopallium.—Closure of the carotids with clamps under ether anæsthesia. Then 0·04 bulbocapnine hydrochloride was given subcutaneously. Local anæsthesia of scalp. On opening the dura the right cortex appeared hyperæmic and fluctuated. The right ventricle was one huge cavity filled with slightly turbid fluid. The right striatum and thalamus were flat. The cortex and the remainder of the corpus callosum were removed, as well as the right choroid plexus. There was only moderate hæmorrhage; the skin was closed with clamps.

Soon after the operation the animal became restless and mewed. Half an hour later the carotid clamps were opened. In the evening all four legs had an increased extensor tone. They all moved. There was a nystagmus to the left and the head and body turned to the left.

September 28: Animal lay on its left side, was apathetic and could not stand or rise. When brought into the right recumbent position the head was raised and the body curved to the left. The animal still had some nystagmus.

September 29: Drank milk well. Could sit up if supported on the left side. The eyes occasionally showed nystagmoid movements to the left. There was definite spontaneous hippus of the pupils. The animal moved the nostrils when the head was brought over the jar of milk. Before urinating she moved around actively.

September 30: The scar fluctuated; by puncture a few cubic centimetres of bloody spinal fluid were removed.

October 1: Fluid had again accumulated and was removed by puncture. The animal walked better. She had an astonishing thirst and great hunger, never refused food and immediately started to lick and swallow as soon as the jar with food came within range of her nose. She urinated so frequently that the floor of her room was flooded.

October 2: Gait and station were unsteady. The animal sometimes fell when she shook her fur. She ate and drank hungrily, and wandered restlessly about as soon as the food was removed. The pupils reacted to light, and the eyelids were closed when a bright light was used. Sometimes the forepaws crossed by mistake and the animal tried in vain to bring them into the right position. When she started to walk the four extremities trembled exactly as the right extremities after the first operation. The tremor gave one the impression that the animal wanted to shake off some heavy object that clung to her paws. The shaking extremity was always raised from the ground.

October 6: Weighed 2·1 kg. After dinner the animal licked her forepaws and wiped her head with the left forepaw.

October 9: The animal had diarrhœa for some days, probably because she ate too much. She was therefore given cocoa, which she disliked, instead of milk. She purred when brushed and while eating. The shaking movements of the paws had almost disappeared, but still occurred if the animal stepped into fluid; then the wet paw was shaken. The animal sat symmetrically; the body-righting-reflex-on-the-body was prompter from the right recumbent position than from the left. The animal usually walked straight forward without any tendency to circus movements. The light reflexes of pupils and of the eyelids were present. The animal opposed every attempt to turn it over on its back. The tonus of the extremities in the recumbent position was symmetrical. There were definite tonic neck-reflexes-on-the-extremities, but no tonic labyrinth reflex could be demonstrated. The neck-righting-reflex was present to both sides. The labyrinthine reflexes on the head were positive. Turning reactions of the head and of the eyes were present, also the "Sprungbereitschafts-reflex." The "lift" reactions were feeble.

October 16: The animal was very active; its gait was still unsteady, especially the hind limbs. The nose was carried near to the floor. She usually walked along the wall, and as soon as she met an object she turned around. At one corner in the fence there was a gap into which the animal often got her nose. Sometimes she spent minutes in this corner moving her nose up and down. Occasionally she jumped, and once succeeded in jumping over the fence which was about one metre high. As soon as she approached a jar filled with food she stopped and started licking movements; she often licked her paws or the floor; when she finally succeeded in reaching the food, she started to eat reflexly. When by chance the metal wall of the jar came between her teeth she bit vigorously on it. She was very particular about her food, disliked cocoa in her milk, but drank pure milk greedily. She preferred fish to other food. Sometimes she licked her forepaws, the fur of her shoulder, or even brought her hindlegs up towards her head to be licked. As a rule these cleaning movements failed, because her tongue was not brought to the desired part of the body, or was applied to some object which was met by chance, like the leg of a chair. These licking movements could always be produced reflexly by brushing the fur.

When the animal met another cat she stopped, smelled at her and might start to lick her, but no chewing or swallowing movements occurred. The animal often slept and then did not react to ordinary sounds. While awake she was extremely sensitive to sounds, the breath of the examiner was sufficient to cause a rotation of her head. As soon as the door of the fence was opened she mewed and started to run around.

October 21: The animal was demonstrated to the Boston Society of Psychiatry and Neurology.

October 25: The animal gave the impression of having some optic reactions. She was examined during the night in a long corridor, the walls of which were greyish brown, the examiner wore a white coat and the corridor was slightly illuminated by a few electric bulbs. When the examiner walked around the animal at a distance of two metres, or changed his position even at a distance of five metres, the animal followed him with her head and eyes. Every step of the examiner to the right or left was followed, and after some time the cat even walked towards the examiner and reached his shoes. As long as the examiner did not move the animal did not look towards him. There was no other evidence that the animal could recognize objects by vision. If there really were a visual reaction, it could only be a reaction to movements within the visual field. These reactions were observed several times, but were only elicited when the animal was sitting quietly. When engaged in any other occupation, as licking, eating or walking, she ignored the movements of the examiner.

When blindfolded the animal's behaviour was strange; she moved her head up and down and apparently licked the inner side of the blindfolder. At the same time she extended her forelegs more and more until she finally lost her balance and fell backwards; then she rose again and repeated the same series of movements. She could not be induced to advance a single step; finally the head sank to her side and the cat seemed to fall into a sleep. After removal of the blindfolder, she immediately started to run around.

The cat performed cleaning movements better. She spontaneously licked her sides, back and paws, but she still performed many useless licking movements in the air. On awaking from sleep she often made typical stretching movements, first stretching the forelegs and then the hindlegs in an exaggerated way.

November 15: The movements of the animal were recorded in an "activity cage."

November 28: For a few days the animal's behaviour changed completely. She was very excited and cried furiously at the slightest touch, bit into the air, scratched furiously the floor and made various sounds, as hissing and screaming, indicating anger and excitement.

December 1: A few nematodes were found in her fæces. A worm cure led to the evacuation of a lot of worms.

December 4: Animal had changed back to her old behaviour. She was again friendly, mewed instead of hissing and did not become excited when touched.

December 5 to 8: She was again placed in the registrating "activity cage."

December 9: The animal spent the greatest part of the day cleaning her fur. While engaged in this she forgot everything else; she did not stop licking when brought into a recumbent position, which usually produced intensive defence movements: she even went on licking when she was hung over a gate in a very uncomfortable position. The reaction to acoustic stimuli had diminished. Licking could be reflexly started by brushing or patting the back.

The co-ordination of the movements of mouth and tongue with the different parts of the body and the extremities had improved, but the animal still never succeeded in licking exactly the point where it had been scratched.

December 11 to 13: The animal was again examined in the registration cage, but had to be taken out on the 13th because it once more changed into a furious and excitable state. The slightest noise made the cat jump forward and attempt to bite and scratch with extended claws. Every object met on her wanderings, as the leg of a chair or empty vessel, was attacked in this way. She had developed mange on her head and her body and was given sulphur inunctions.

December 18: Mange was healed. The cat was put back in the registration cage.

December 20: The animal seemed to have a certain sense of location; for instance she sat near the bowl filled with food which was attached to the wall of the cage at the level of her head, and every time she wanted food she lifted her head, turned it to the left and brought it to the bowl. While chewing she withdrew her head, but afterwards brought it back directly to the bowl.

December 31 to January 3: Another examination in the registration cage.

January 3: The basal metabolic rate was determined when the animal had fasted for twelve hours. Weight 2·54 kg. Temperature 101·9° F. Metabolism 2·615 k. per kg. an hour.

January 6: When fasting for twenty-four hours weight was 2·54 kg., temperature 101·8° F., metabolism 2·51 k. per kg. per hour.

During February and March many experiments were made on the nystagmus of the eyes on rotation. These experiments are reported in a special chapter. On the whole the behaviour of the animal did not change, but she gradually became quieter and less active than during the first few months after the operation.

March 18: The weight of the animal was 2·9 kg. The cranial cavity was opened under bulbocapnine and local anæsthesia, and the remaining part of the brain was examined by electrical excitation. This experiment is reported in a special protocol. After this experiment the animal was killed.

Summary of Protocol 2.

The left neocortex was removed on August 4, 1926. After recovering from the first operation she developed, at the end of September, an apathetic state which was apparently due to an increasing hydrocephalus; therefore the second operation, which consisted in removing the right neocortex, was performed on September 27. The animal stood the second operation very well. A peculiar phenomenon during the first days after the operation was a clonic shaking of the extremities when the animal started to walk after a period of rest. These shaking movements had already been observed after the removal of the left hemisphere, but then only on the right side. After a few days these shaking movements disappeared and only reappeared when the animal wet or soiled its paws.

In its best period the animal was active and moved about all day. The muscle tone and all the righting reflexes were normal; but the hind-legs were somewhat unstable and she walked with a wide base and swayed. Isolated movements of each forepaw were observed repeatedly, especially rubbing the eyes when these were closed with adhesive plaster. One of the most striking performances was cleaning the fur, and the way in which this was relearned was interesting. In the first attempts at licking the movements of the tongue and lips were excessive and accompanied by large and inappropriate movements of the head. Later, parts of the body were brought up towards the head and tongue, and finally the animal really succeeded in licking its body effectively. Until the end the animal made mistakes, and would lick the floor or the wall if it met them by chance during the cleaning procedure.

The animal ate spontaneously and found its food by smell. It showed preference for certain foods and especially for fish and milk. The hunger and the thirst of the animal were pathologically increased, especially during the first weeks after the operation. If the animal was left alone with sufficient fluid and food it would eat and drink continuously, and in consequence of this it would urinate at short intervals and get diarrhœa. The amount of fluid and food had to be therefore restricted.

The animal was very sensitive to sounds and turned the head even at the snapping of a finger-nail. It always started to move and mew when the door was opened. She did not recognize objects by vision, but exposure to light caused contraction of the pupils and blinking of the eyelids. In several experiments we had the impression that she followed with her eyes and head the examiner when he moved. This suggests that perhaps movements were perceived by vision, but of this we cannot be certain as the animal was able to hear.

Kleopatra could produce a varied scale of sounds, from the pitiful mewing which occurred every time the door was opened, to furious crying, hissing and spitting which she produced in disagreeable situations. It is of special interest that she showed different moods. In general she was gentle, but during two periods, each lasting several days, she was very excitable and reacted with definite signs of anger to every stimulus. During the first period nematodes were found in the stools and after they were eliminated the excitability disappeared. During the second period the animal suffered from mange.

The animal had a tendency to stereotyped motor performances, as eating and cleaning her fur. During these she was so much occupied that she reacted much less to external stimuli than usual.

RECORDS OF ACTIVITY OF THE CAT WITHOUT NEOCORTEX.

We measured the animal's activity by means of a special apparatus. The floor of one of the usual wire observation cages (about one metre in each dimension) was suspended by steel springs and the movements of one of its corners were recorded on a kymograph. The cage was placed in a separate room and was visited and cleaned only once a day. Urine was collected through a funnel. Observations were made for periods of forty-eight to seventy-two hours on seven different occasions, totalling nineteen days.

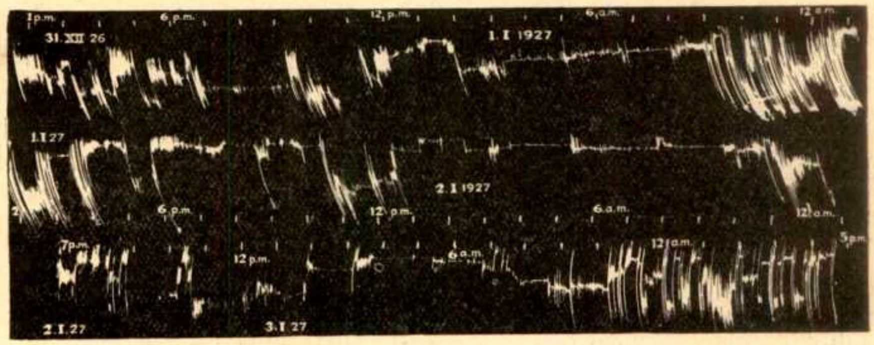

FIG. 3.

One of the records, extending over three days, is reproduced in fig. 3. These tracings show the tremendous activity of the animal, which is particularly striking when compared with that of a normal cat observed under the same conditions (fig. 4). The normal cat was relatively quiet; about every two hours it walked around a little, but soon settled down again. Kleopatra, however, was always on the move by day; during the night she was quieter, but still was more restless than the

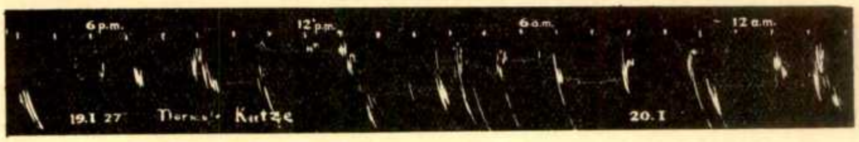

FIG. 4.

normal cat. The striking difference in her behaviour during day and night cannot have been due to the daylight, as this was excluded from the room. The only changes between day and night were the noises from outside. As a matter of fact the tracings of the animal's activity corresponded to the activity of the college, which was greatest between 9 a.m. and 6 p.m., when footsteps, voices in neighbouring laboratories, the opening and closing of doors, &c., were constantly audible. We conclude that noises had a very important influence on the animal's motor activity.

On the two occasions when the animal was excitable and ill its behaviour was different. Fig. 5 shows a record of two days while it suffered from mange. The tracings by day differed little from those usually obtained, but she rarely rested by night, in fact between midnight and 6 a.m., when she was usually quietest, the record resembles closely a day-time tracing. This was probably due to the unpleasant stimuli excited by the mange and the gastro-intestinal parasites.

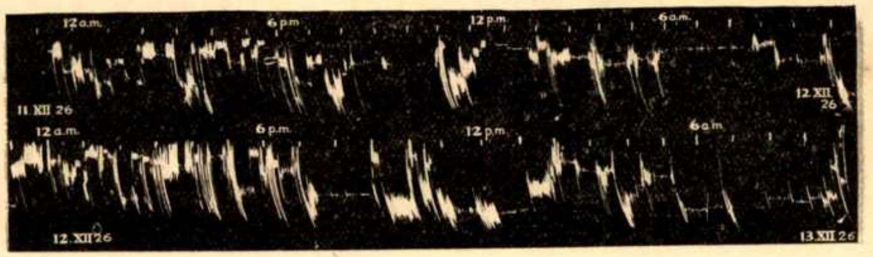

FIG. 5.

We tried to determine whether light or darkness had any influence on the animal's behaviour. The cat was usually in complete darkness while in the observation cage, but one day the room was illuminated by a 100-candle bulb. On another occasion the room was dark during the day and lit up at night. Finally, we tried to see if the animal reacted when the light was turned on and off. None of these experiments caused any significant change in the animal's behaviour.

STUDIES ON ROTATIONAL NYSTAGMUS AND AFTER-NYSTAGMUS IN THE ANIMAL WITHOUT NEOCORTEX.

Nystagmus during rotation has been studied by direct observations in man (Bárány), but its control by animal experiments has been comparatively neglected. One of the reasons for this is the technical difficulty of observation during rotation ; another is the interference by optical influences, which can excite nystagmus by mere rotation of the visual field. Recent work by Stenvers and Holmes indicates that this optical nystagmus depends on cortical reflexes. Therefore it seemed that an animal without cortex ought to be an interesting subject for the investigation of nystagmus during rotation. There is the further advantage that in such an animal the complicated "voluntary" reactions of the cortex do not disturb the observations.

To compare nystagmus during and after rotation we built a special rotating wheel on which the cat could be fixed in any position. An arrangement of three mirrors made it possible to keep the eyes of the animal, which were illuminated by an electric lamp, under observation while the wheel was rotating. The wheel was moved by hand, and regulated by the beats of a metronome, so as to assure a fairly constant speed.

In testing the reactions of the labyrinths different factors have to be considered.

(1) The "speed of the rotation" is expressed by the "rotation quotient." This is the number of rotations per minute if the rotations were continued indefinitely.

(2) "Acceleration," which means alteration of speed during a unit of time. This comes into play at the start and at the stop of the rotation. Unfortunately we were not able to measure it, but we have assumed that both the start acceleration and the stop acceleration increase proportionally with the speed of rotation. There ought to be no acceleration between, but there can be little doubt that some of the irregularities in our observations were due to changes in the rate of rotation. Exact experiments would require that accelerations could be controlled and recorded mechanically.

One effect of the rotation is a nystagmus which starts after a short latent period; the first few jerks are small and quick, then they become large in amplitude and equal, and finally the nystagmus gradually disappears, the individual jerks occurring at longer and longer intervals. The latency of the nystagmus can be observed especially when rotation is stopped, as then a jerk in the direction of the rotational nystagmus may be observed before nystagmus in the opposite direction develops. As the nystagmus fades out slowly, its duration in seconds is not an accurate measure of its intensity. The number of the nystagmus jerks is a better criterion. There may be, for instance, fifty jerks while a control may have fifty-one jerks, but the last jerk may come ten seconds later and thus change the duration of the nystagmus by 20 per cent. We have, therefore, paid little attention to the duration of the nystagmus.

The following questions were studied :—

(1) What effect have different numbers of rotations at a given speed on the number of the nystagmus jerks?

(2) What effect have differences in speed, the number of rotations being constant, on the number of jerks?

We studied these two questions both in the nystagmus during rotation and in that occurring after rotation. Observations were made on rotational nystagmus at different speeds up to thirty revolutions a minute, and for as many as four revolutions. After-nystagmus was studied more extensively. The experiments were performed during February and March, 1927; the excitability of the animal during this period declined considerably, and especially on March 15 to 16, perhaps owing to sores which had developed on the knees. The observations made on March 16 are not therefore included in our curves, but the figures can be found in the tables. On this date the nystagmus had a very long latency, especially the nystagmus during rotation, but the latent time of the after-nystagmus was less.

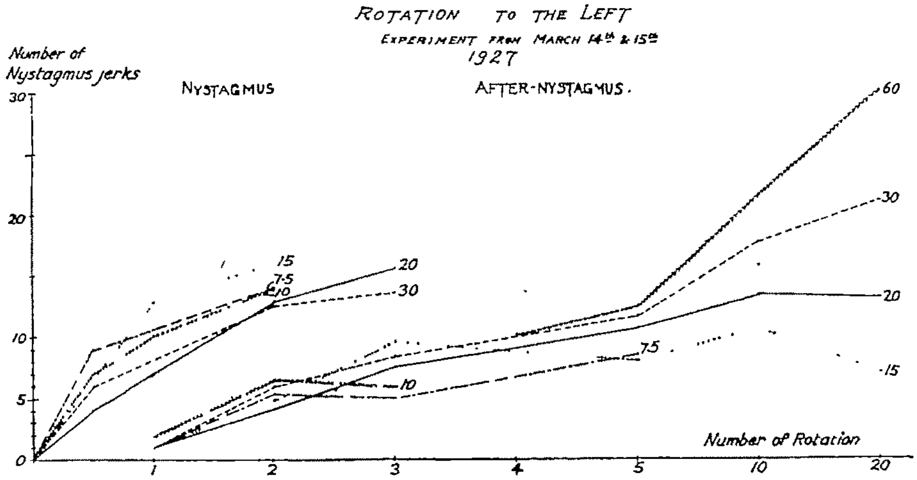

FIG. 6.

The following tables give the results of all the experiments. Each figure is usually the average of three or more measurements. The observations can be understood more easily by looking at the curves constructed from these figures. As the results of rotation to the left and to the right were practically the same, it is sufficient to consider rotation to one side only.

Fig. 6 contains two groups of curves, the left representing rotational nystagmus, the right after-nystagmus. Every curve represents a constant speed of rotation and shows the relation between the amount of rotation and the number of nystagmus jerks for this speed. They show that definite after-nystagmus starts only after one complete revolution, while the rotational nystagmus starts immediately.

The number of after-nystagmus jerks reaches the number of rotational nystagmus jerks produced by 45° of rotation only after three complete revolutions at the same. speed. During speeds of 7½ to 60 revolutions a minute the curves are similar as long as the amount of rotation is small; but after more rapid rotation the curves of the after-nystagmus vary according to the speed. Probably the same effect could be demonstrated for the rotational nystagmus, but it was not possible to count it during more than three or four rotations. Figs. 7 and 8 show that rotational and after-nystagmus depend on the speed of rotation; each curve represents a single rotation. When the speed of rotation exceeded 30 per minute the rotational nystagmus could not be counted, but after-nystagmus was counted up to 60 rotations per minute. Rotational nystagmus was very irregular at a speed of 7·5 revolutions per minute, because slow movement could not be kept up without acceleration. At speeds of 10, 15 and 20 revolutions per minute the number of jerks depends largely on the amount of rotation; 180° of rotation produces more jerks than 90°, 360° more than 180°, and so on. The diagram shows that the number of jerks produced by a certain amount of rotation is more or less constant at various speeds.

The curves of after-nystagmus show a similar behaviour (fig. 8). At medium speeds the number of jerks depends chiefly on the amount of rotation, not on the speed. This is true, however, only as long as not more than 4 to 5 revolutions are performed. With more revolutions the nystagmus varies with the speed of rotation; the higher the speed, the more the nystagmus increases proportionally to the amount of rotation. The results of these observations are:—

(1) With small amounts of rotation (below 360°) after-nystagmus is negligible.

(2) With small amounts of rotation the number of jerks is, within certain limits, independent of the speed of rotation, but depends on the amount of rotation.

(3) Definite after-nystagmus develops only after 360° of rotation.

It is only after three or four revolutions at least that the numbers of jerks of rotational nystagmus and after-nystagmus depend essentially on the speed of rotation.

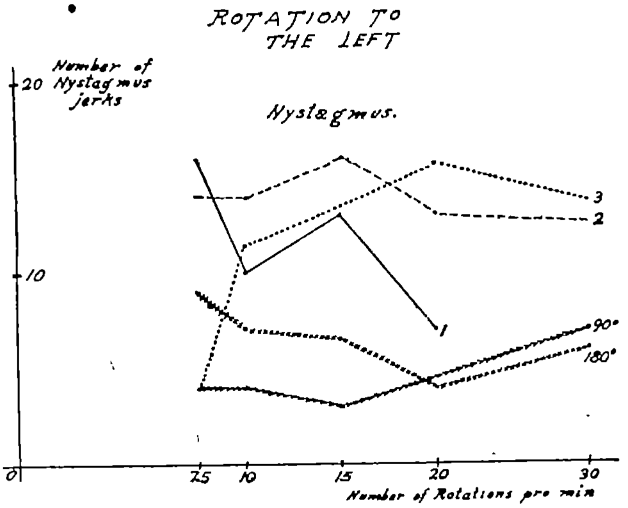

FIG. 7.

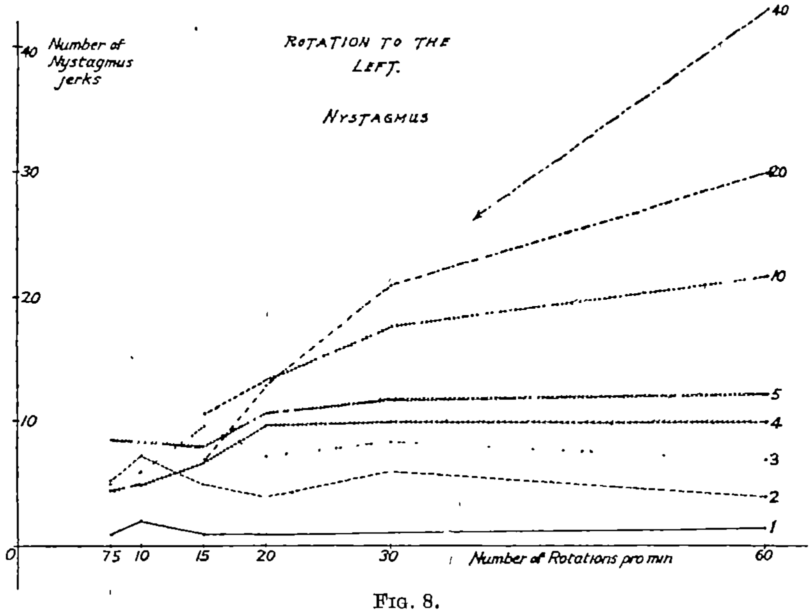

FIG. 8.

Within a certain range the nystagmus corresponds, therefore, to the amount of rotation in space; beyond this range it behaves differently. If the acceleration is too small the stimuli it excites are below the threshold of the labyrinth. When the amount of rotation is increased, acceleration is the chief determinant of the number of jerks, and the labyrinth no longer reacts to the rotation alone. These facts are important because the amount of rotation that excites a reaction is within the range which occurs commonly during the natural movements of the animal. The reactions to acceleration, beyond this range, are reactions to non-physiological stimuli. They may be useful for the otologist, but they are a disadvantage to the animal. This statement of course holds good for rotational nystagmus only ; it is obvious that the maintenance of equilibrium needs physiological reflexes to acceleration.

These observations corroborate entirely the earlier observations of Mach [10], Breuer [3], Brown [5], Bárány [1], Masuda [13], and others on intact man and animals. They prove that the forebrain is unnecessary for all those features of rotatory nystagmus and after-nystagmus which have been described.

Our observations add nothing new to the theory of the functions of the labyrinth. They are compatible both with the older theory of Breuer [3] and Brown [5], that the labyrinthine reactions correspond to a real movement of the endolymph : and with the more recent theory of Mach [10] and Bárány [1], that the cupula of the labyrinth reacts only to acceleration, and that this reaction excites a mechanism in the nervous system which causes the nystagmus, and which can be inhibited by an impulse of the opposite direction if it appears before the mechanism has completely discharged.

The fact that rotational nystagmus, within certain limits, represents a reaction to the amount of rotation seems of special importance. During rotation these movements of the eyes dissect the panorama into a series of pictures, each of which is exposed to the retina for a moment. We know that the retina reacts for a certain time to every beam of light, so each picture must be fixed long enough to avoid confusion with the after-excitation of earlier images and with the excitation of the next. The gap between the separate pictures is compensated by the fusion of a series of images exposed one after another into the perception of "movement," the principle on which cinematography depends. Without nystagmus the objects could not be fixed long enough to leave a sharp picture on the retina; vision would be indistinct and points would appear as lines whenever we rotated.

Our experiments seem to suggest that the number of pictures into which the panorama is divided during rotation does not vary much at different speeds. The teleological aspect of the problem allows one to predict that this will not be true with greater speeds of movement. There is an "upper limit" of the latency of the nystagmus jerk adapted to the duration of the after-discharge of the retina. If the interval becomes shorter than this we would get double and triple pictures of moving objects, just as one does when moving objects are illuminated with a spark. This, as a matter of fact, seems to happen under pathological conditions only.

7·5 REVOLUTIONS PER MINUTE.

Rotation to the right				Rotation to the left			Date
Rotation	Nystagmus	After-nystagmus	Duration	Nystagmus	After-nystagmus	Duration	
90°	4			4			Feb. 7
180°	9			9			,, 12
360°	15	1		16	1		,, 12
2	8	7	4	14	5¼	6¼	Mar 14
3	8¼	3	2	4	5	8	,, 14
4	6½	3⅔	5	4	4½	4	,, 16
5		6	5½		8½	6½	,, 15

10 REVOLUTIONS PER MINUTE

Rotation to the right				Rotation to the left			Date
Rotation	Nystagmus	After-nystagmus	Duration	Nystagmus	After-nystagmus	Duration	
90°	3			4			Feb 7
180°	7	(1)		7	(1)		,, 7
1	11	2		10	2		Mar. 14
2	13¼	6⅓	4	14	7¼	5	,, 14
3	12¼	7	5¼	11½	6	4⅔	,, 14
4	3	3	8	4	5	5	,, 16

15 REVOLUTIONS PER MINUTE.

Rotation to the right				Rotation to the left			Date
Rotation	Nystagmus	After-nystagmus	Duration	Nystagmus	After-nystagmus	Duration	
90°	3			3			Feb. 7, 1927
180°	6½	(1)		6½	(1)		,, 7, 1927
360°	13	(1)		13	(1)		Mar. 12
2	14	5¼	4½	16	5	4½	,, 14
3	13	7⅓	4½	13¼	9⅓	5⅓	,, 14
4	9	7	6⅓	8¼	6¼	7	,, 16
5		7¼	5¼		8	6½	,, 12
10		8¾	6½		10¾	8	,, 15
20		8	6		7	6½	,, 15

20 Revolutions per Minute.

Rotation to the right				Rotation to the left			Date
Rotation	Nystagmus	After-nystagmus	Duration	Nystagmus	After-nystagmus	Duration	
90°					(1)		
180°	3½	(1)		4	1		Mar. 14
360°	6	1		7	4		,, 14
2	13	3½	2	13	7⅓	2⅕	,, 14
3	15⅔	5	2⅔	15⅔	9¾	4½	,, 14
4	13	9	7	11⅓	10⅔	8	,, 16
5		10⅔	7⅕		13⅓	7¾	,, 15
10		10	8⅔		13	8½	,, 15
20		12½	9			9½	,, 15
40							

30 Revolutions per Minute.

Rotation to the right				Rotation to the left			Date
Rotation	Nystagmus	After-nystagmus	Duration	Nystagmus	After-nystagmus	Duration	
90°	5			7			Feb. 7
180°	6	(1)		6	(1)		,, 12
360°			3			4	Mar. 12
2	11⅓	5	5	12½	6	6	,, 14
3	13½	6	5½	13⅔	8⅓	6⅔	,, 14
4	12⅓	8⅓	7⅓	13⅔	10	7	,, 16
5		13	8½		11⅔	10	,, 15
10		16	10½		17¾	12	,, 15
20		17	12		21	12⅕	,, 15
40							

60 Revolutions per Minute.

Rotation to the right				Rotation to the left			Date
Rotation	Nystagmus	After-nystagmus	Duration	Nystagmus	After-nystagmus	Duration	
90°							
180°							
360°		1½	2		1½	2	Mar. 16
2		4	3¾		4	4½	,, 16
3		6½	5¼		7	5¼	,, 16
4		8⅓	6¾		10	6¾	,, 16
5		12⅓	7½		12⅓	7½	,, 15
10		21	10¼		21⅔	10½	,, 15
20		27	14		30	14	,, 15
40		47	18		43	19	,, 16

ELECTRICAL EXCITATION OF THE REMAINING BRAIN (MARCH 18, 1927).

The animal received 0·45 gr. of bulbocapnine hydrochloride subcutaneously; later in the course of the operation 0·04 gr. was given; the scalp was infiltrated with 1 per cent. novocain solution and the skin was cut in an X-shaped incision. The temporal muscles were separated easily on both sides from a dura-like connective tissue membrane which was adherent to the longitudinal bridge of bone which was left at the former operations; it was dissected from this bridge. After this a transparent cystic mass which contained fluid appeared on both sides of the bridge. This apparently consisted of dilated arachnoidal spaces filled with cerebrospinal fluid. Nervous tissue could be seen in the floor of these cysts. The dura was lightly attached to the walls of the cysts,

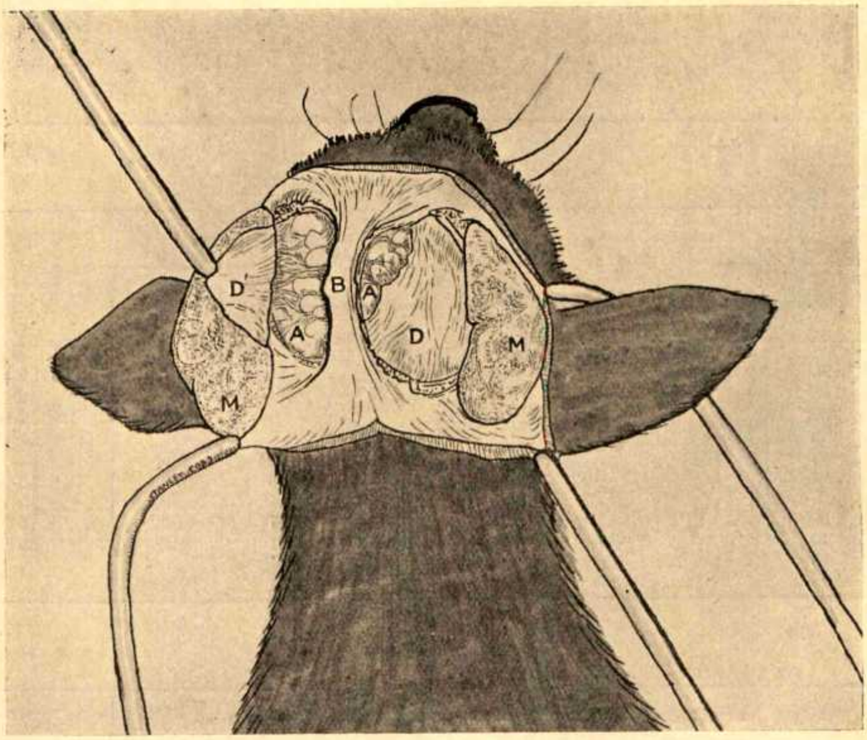

FIG. 9.—Appearance of the skull and of the brain at the first stage of the biopsy. A, arachnoidal cyst. B, arch of bone. D^1, the dura which has been reflected back. D, dura in place as exposed. M, muscle which has been dissected from the skull.

but could be separated from them (fig. 9). The bridge of bone was then removed, and below it a thick band of connective tissue, which corresponded to the sagittal sinus and falx, was found. This band was dissected at the frontal end, and carefully reflected towards the occipital bone. The cysts on both sides collapsed owing to small punctures in the arachnoid. The arachnoidal tissue was incised and this exposed two huge cavities with flat walls. The last part of the operation had to be performed under ether anæsthesia, as the cat became very restless whenever the dura-like membrane was touched. The entire operation lasted an hour and a half.

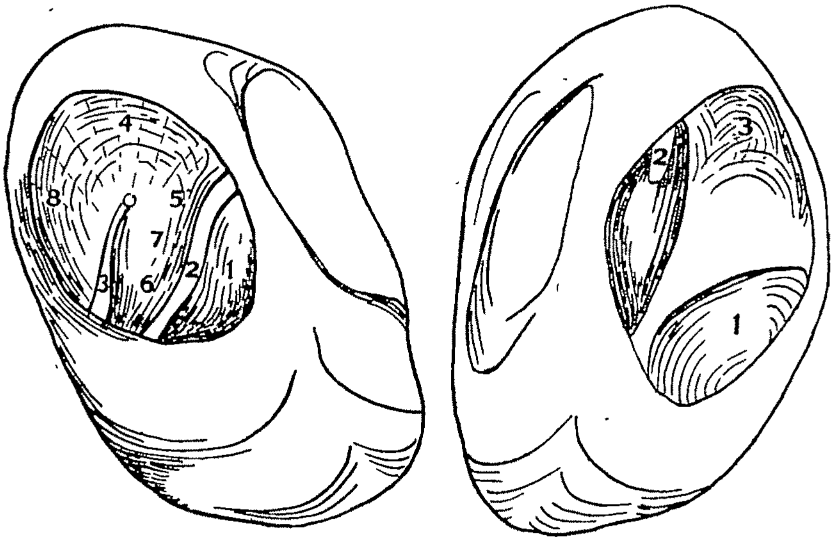

Fig. 10 (Compare with fig 11A).—These drawings of the cysts show the areas which were stimulated and later identified by microscopical examination.

A sponge soaked with saline was placed in each of the open cysts. Between noon and 2.30 p.m. the animal gradually recovered; at 2.30 she was able to walk fairly well. She was hung in a towel in which holes had been cut for the four extremities; the electrical stimulation was then begun. Periodic motor discharges were observed, independent of electrical excitation; these were accompanied by dilatation of the pupils and acceleration of the respiratory rhythm. Tremors also appeared spontaneously from time to time.

Reactions to Electrical Stimuli (compare fig. 10).

2.45 p.m.—Animal hanging in the towel. Making slow walking movements with her forepaws; claws expanded on all four legs; head turned to left; respiration rapid, 48.

2.29 p.m.—Wound is opened. Removal of cotton from right cyst. Alternating movements of forelegs.

2.31½ p.m.—Stimulation of posterior part of mesial wall of right cyst; 10 cm. distance of coils. Alternating movements of forelegs; more tonic extension of right leg.

2.33 p.m.—Stimulated again: nothing new.

2.34 p.m.—Stimulated with coils 7 cm. apart; no reaction.

2.35 p.m.—Stimulated on outer surface (point 1).

2.36 p.m.—Stimulated anterior to point 1; no change.

Later tonic reaction, turning head to right.

2.40 p.m.—Point 1; winking movements of both upper lids, especially left, a short time after stimulation.

2.42 p.m.—Point 1; tonic turning of head to right.

2.42½ p.m.—Point 1; winking of both upper lids, and as an after-effect tonic turning of head to right and high stepping of forelegs.

2.43 p.m.—Stimulated again. Point 1; winks both upper lids.

2.44 p.m.—Stimulated again. Point 1; winks both upper lids.

2.48 p.m.—Stimulated Point 2 (9 cm.) in anterior part of middle of mesial wall of right cyst; deep and rapid breathing.

2.49 p.m.—Same.

2.50 p.m.—Stimulated Point 2 (13 cm.); no reaction except movement of foreleg.

2.52 p.m.—Stimulated Point 2 (10 cm.); urination.

2.53½ p.m.—Stimulated Point 2 (9 cm.); superficial and rapid respiration; urination (this continued a few seconds after stimulation).

2.54 p.m.—Stimulation repeated; deep, long respiration.

2.56 p.m.—Stimulation repeated; increased respiration and a good deal of movement.

2.57 p.m.—Stimulation of Point 3 (9 cm.) in anterior end of cyst; no effect.

2.57½ p.m.—Stimulation of Point 3 (9 cm.) in anterior end of cyst; no effect.

On handling head afterwards (raising chin), marked tremor of both forelegs.

2.59 p.m.—Stimulation of Point 3 (9 cm.); the right leg twice made long goose-step movements. More movements half minute afterwards.

3.1 p.m.—Touching head to sponge out cyst: increased respiration.

3.1½ p.m.—Stimulation of Point 2; rapid respiration.

3.2½ p.m.—Stimulation of anterior end of mesial wall; no effect.

3.3½ p.m.—Stimulation (9 cm.) of anterior end of lateral wall; alternating movements of forelegs and more rapid breathing.

3.5 p.m.—Repeated, same results.

3.6 p.m.—Raising head without stimulation causes a few movements.

3.6½ p.m.—Further raising of head, same result.

3.7 p.m.—Stimulation of anterior part of mesial wall; movements of forelegs immediately.

3.8 p.m.—Stimulation of Point 1; winked once; tonic turning of head to right.

3.8½ p.m.—Stimulation repeated; no winking, but moving of legs and turning of head to right.

After effects: more running movements of legs than before stimulation.

3.11 p.m.—Stimulation of Point 1 (9 cm.), several times; alternating movements of leg; head turned to right; right hindleg moved a few times.

3.13½ p.m.—Stimulation of Point 2 for 25 sec.; increased respiration. After-effect: two squawks.

3.14¾ p.m.—Stimulation of Point 2 twice in succession; no effect.

3.16 p.m.—Stimulation of anterior part of mesial wall for 15 sec.; no change in legs.

3.16½ p.m.—Stimulation of Point 1; slight winking of eyes.

3.16¾ p.m.—Same, repeated 3-4 times; same results. After effects—spastic stepping movements; no turning of head; marked walking movements of forelegs

3.18 p.m.—Stimulation same; no results while the current was on. After-effects same as above.

3.18½ p.m.—Stimulation of Point 1 (9 cm.); nothing. After-effects: running movements, lifts legs as high as nose; cried.

3.20 p.m.—Stimulation same; rapid respiration.

3.22 p.m.—*Left* cyst opened and right one closed with plug of cotton-wool. High reaching with forepaws; head to left; tremor.

3.24½ p.m.—Stimulation of Point 1 behind posterior wall of cyst (9 cm.); high stepping and head turned to left.

3.25 p.m.—Stimulation same; no effect; cried afterwards.

3.27 p.m.—Stimulation of Point 2 (9 cm.) on medullated line on floor of left cyst, licking movements; left facial contractions; puckering of nose.

3.28 p.m.—Stimulation same; previous movements repeated. After-effects (1 min.): epileptic attack; tongue to left; biting movements; salivation, head to left; tongue in and out.

Separation of coils to 12 cm.

3.31½ p.m.—Stimulation of anterior part of bundle; forepaw flexed.

3.32 p.m.—Stimulation of posterior part of bundle; no effect.

Coils again separated to 9 cm.

3.33 p.m.—Stimulation of anterior part of bundle; licking and movements of mouth.

3.34½ p.m.—Stimulation of posterior part; licking in midline.

3.34¾ p.m.—Stimulation of anterior part; movement of nose; tongue out in midline After-effect: became sleepy.

3.36 p.m.—Stimulation repeated; left lip moved first and then right lip.

3.37 p.m.—Stimulation in angle between anterior wall and floor of cyst; no effect on legs; respiration a little more rapid. Repeated with same results.

3.41 p.m.—Stimulation of Point 3; cried once, respiration more rapid; both eyes moved down.

3.41½ p.m.—Stimulation repeated.

3 p.m.—Repeated.

3.47 p.m.—Stimulation of Point 4 in roof of cyst: no effect (perhaps slight jerking of eyes).

3.49 p.m.—Stimulation of Point 5 (mesial part of grey mass on floor): animal absolutely quiet. After-effects: few licking movements; turned head to left; stepping a little.

3.51 p.m.—Stimulation repeated; stepping movements; cried; pupils dilated.

3.52 p.m.—Stimulation repeated; turns head far to left.

3.53 p.m.—Stimulation repeated. After-effects: running movements and elevation of head.

3.54 p.m.—Stimulation of Point 6 (lateral part of grey mass): twitching of left side of face; left eye winked (at this point a slight hæmorrhage occurred); increased respiratory rate.

3.54½ p.m.—Stimulation repeated; same results. Afterwards: running movements.

3.56 p.m.—Stimulation of Point 7 (between 5 and 6); very rapid breathing, with nostrils moving.

3.58 p.m.—Stimulation repeated. Afterwards: breathing stronger and dilatation of nostrils.

3.59½ p.m.—Stimulation of Point 8 (anterior lateral wall of cyst). Afterwards: running movements.

4.1 p.m.—Stimulation same.

4.2 p.m.—Stimulation of Point 6; contraction of muscles of left side of face.

4.4 p.m.—Stimulation of Point 5, a few jerks of both eyes to left.

4.5 p.m.—Repeated. Results same.

4.5½ p.m.—Repeated. Movements of head and eyes to left; left eye-jerks. Afterwards: running movements and head turned from right to left

4.7 p.m.—Stimulation of Point 5 twice; eyes jerked.

Stimulation of Point 5 twice; eyes jerked to left. Afterwards: running movements and cried once.

4.9¼ p.m.—Stimulation same; eyes jerk downwards.

4.12¼ p.m.—Stimulation of Point 6; no effect.

4.13½ p.m.—Stimulation of lateral part of Point 1; no effect.

4.15 p.m.—Stimulation of Point 7; no effect.

4.16½ p.m.—Stimulation of Point 2, left whiskers moved; both lip whiskers changed a little. Afterwards: constriction of both pupils, head rigid.

4.17½ p.m.—Stimulation repeated; champing; tongue moved in and out in midline; whiskers moved. Afterwards: quite rigid.

Returning to Right Cyst.

4.21¼ p.m.—Stimulation of Point 1; no results.

4.21½ p.m.—Repeated. Winking.
Repeated. Winked with left eye.
Repeated. No result.

4.22½ p.m.—Stimulation of Point 2; increase in rate of respiration.

4.25 p.m.—Stimulation of Point 2; marked increase of respiration.

4.26 p.m.—Stimulation same. Not much change.

4.26½ p.m.—Stimulation same. Not much change. Afterwards: strong running movements.

4.27½ p.m.—Stimulation repeated. No result.

Returning to Left Cyst.

4.36½ p.m.—Stimulation of Point 2; whiskers moved; licking; champing: movement of tongue.

4.38½ p.m.—Stimulation of Point 2 (increased current). Champing licking, &c. Afterwards: licking, head turned to left.

4.40 p.m.—Stimulation same. Champing and licking. Spot marked with indian ink.

Return to Right Side.

4.55 p.m.—Stimulation of Point 2. Increased respiration. Spot marked with indian ink.

SUMMARY OF EXCITATION EXPERIMENTS.

In studying this protocol one must take into consideration the fact that periodic discharges of movements took place, a typical phenomenon in cats without the forebrain when they are suspended, as Schaltenbrand and Girndt [17] have shown. These movements may have started by chance, or as the after-effect of electrical stimulation of any point, so they cannot be considered as a definite effect. Twitching of the eyelids and of the face could be elicited behind the right cornu Ammonis; it is doubtful if these were of reflex origin (due to trigeminal irritation) or a result of spread of the electric current to the base of the skull. The animal had also a tendency to rotate its head more frequently to the right while we were working on the left side of the brain.

Definite effects could be obtained from "Point 2" on the left side, which lay over a medullated bundle running to the midline. When this bundle was stimulated the nose was puckered, the whiskers moved, the animal made biting, licking and swallowing movements, and stronger stimulation excited epileptic attacks. Another area from which definite effects could be obtained was "Point 2," on the velum medullare of the right ventricle. Excitation of this point was twice followed by evacuation of the bladder, and repeatedly by irregular changes of the respiratory rhythm.

At the end of the experiment the animal was able to stand and to walk; she was unsteady, however, and more tremulous than usual.

NECROPSY.

When the experiments were completed the animal was anæsthetized with ether and was bled from the femoral arteries. While the heart was still beating the carotids were injected with formalin.

The spinal cord was removed within the dura and left attached to the medulla oblongata. The head was then severed from the atlas. Sponges soaked in formalin were introduced into the cysts, and the head and spinal cord were put into formalin.

On March 20 the bone was removed from around the brain. The pieces of muscle which had been inserted at the operations were densely adherent to the dura, and between them and the cortex there was a reddish mass of jelly-like consistency. The brain was removed easily without damage. The middle ears and labyrinths appeared normal to the naked eye.

Description of the brain (fig. 11).—Some cortex had been left, including on the left side the gyrus proreus, most of the lobus piriformis and a small part of the gyrus fornicatus, and on the right the gyrus proreus, the entire lobus piriformis and the edges of the gyrus ectosylvius and gyrus fornicatus. The cornu Ammonis was visible on both sides. On the left side the choroid plexus could be recognized. The anterior and posterior horns of the lateral ventricles were represented by large cavities. The stimulation experiments had been made in the anterior horn of each ventricle. On trying to lift up some overhanging tissue from the posterior end of the left anterior horn, the brain was torn slightly. The right olfactory bulb had been damaged during dissection.

After being hardened in formalin and alcohol the brain was embedded in celloidin and cut in serial sections. Every fourth section was stained by Nissl's method, and every other fourth section by Weigert's method. The serial sections, which were made by an inexperienced technician, were not perfect, but were sufficiently good for the study of the brain. The sections and the photographs do not bear their serial numbers, but the corresponding Nissl and Weigert sections always bear the same number.

MICROSCOPICAL EXAMINATION OF THE BRAIN.

The first sections pass through the olfactory bulbs and the frontal poles of the brain. The olfactory bulbs are well preserved, but there are central

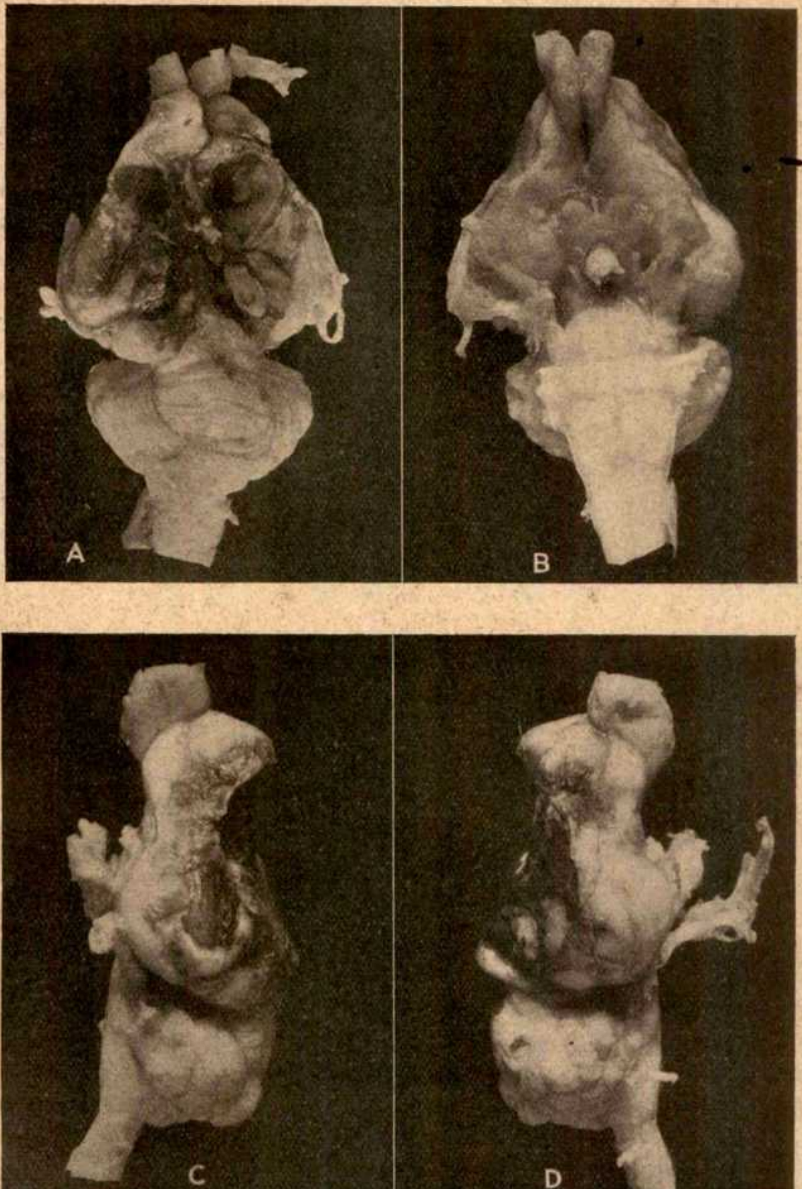

FIG. 11.

softenings around their ventricles. The right frontal pole is larger than the left. The white matter is necrotic and contains cavities which separate the medial and the lateral parts of the cortex.

Section 43 corresponds approximately to plates 1 and 2 of Winkler and Potter's monograph. A good deal of cortex remains in the frontal lobes of both sides, especially in the gyrus proreus and gyrus genualis (fig. 12 Nissl stain). The operative incision followed the sulcus Sylvii and the sulcus cruciatus, leaving only a small part of the gyrus sigmoideus anterior. The cortical cells are well preserved, and a few pyramidal cells can be recognized on both sides. The large cells in the sixth layer have disappeared on the left side, which was operated on first, but are still present on the right. The meninges are infiltrated by cells. Weigert's stain shows that the white matter has disappeared on both sides with the exception of a few arcuate fibres (fig. 13). In both hemispheres the operation has entirely destroyed all fibres which might pass around the ventricles to enter the internal capsules.

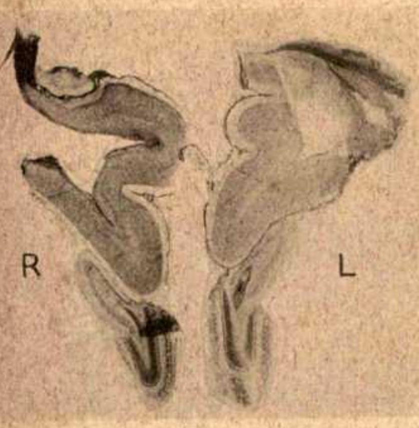

FIG. 12.

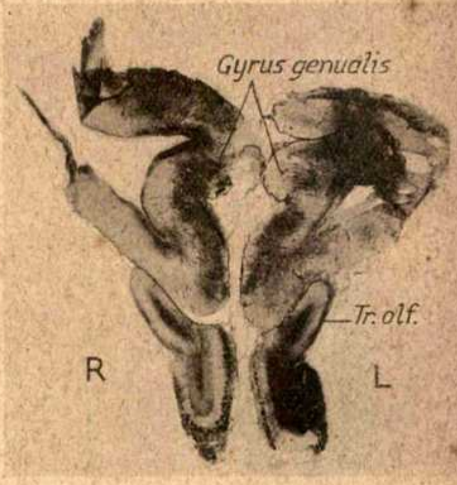

FIG. 13.

Section 60, Nissl stain, shows the brain a little anterior to the genu of the corpus callosum. A necrotic mass of fibres on both sides corresponds to the commissural radiation from the corpus callosum. The only cortex remaining is a small portion of the gyrus rostralis above this mass and the gyrus genualis below it. The olfactory tract, which has united with the brain, is well preserved on both sides. On the left side a small portion of the area 13 of Winkler and Potter remains in the depth of the sulcus præsylvius, but on the right there is only a very thin layer. Some large cells above this layer might correspond to the oral part of the claustrum. The caudate is not yet visible, and there is no indication of the capsular radiation of the frontal cortex. In the Weigert sections the tapetum appears degenerated.

Section 78 passes through the necrotic genu of the corpus callosum (fig. 14, *G. c.c.*), which is collapsed and folded; below it a dark line of cells on both sides represents the nucleus medullæ terminalis. On the right side the pole of the caudate is separated by the necrotic internal capsule from what seems to be the putamen. A few myelinated fibres in the capsule belong to the striothalamic radiation. The parts of the cortex preserved are the same as in the more anterior sections. Laterally the brain extends out on each side to

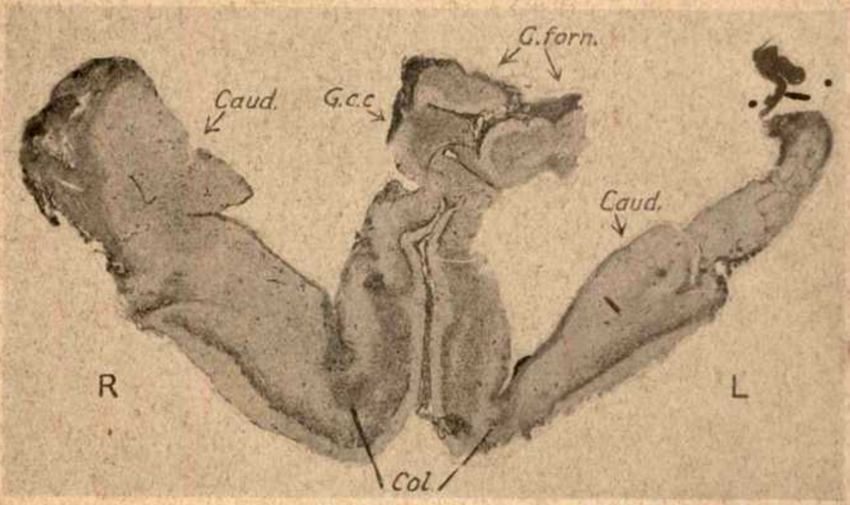

FIG. 14.

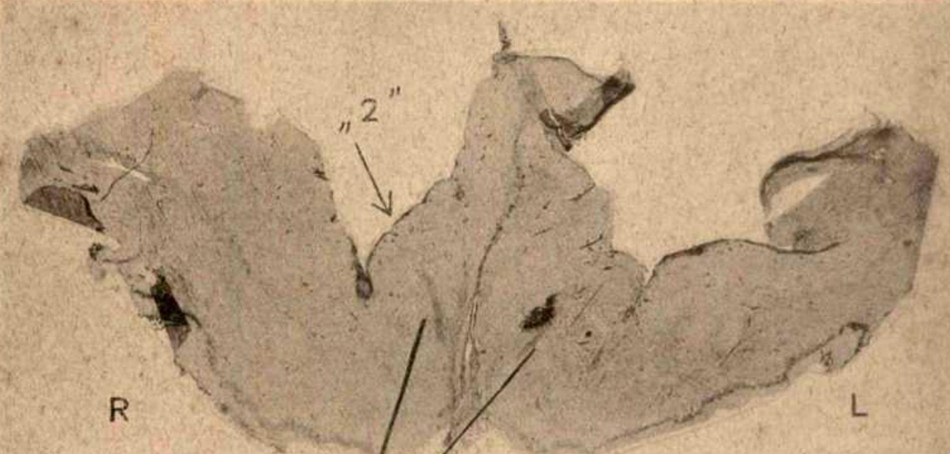

FIG. 15.

the necrotic gyrus orbitalis. The anterior end of the striatum is preserved to a great extent on the right side, but on the left the caudate only can be recognized. The colliculum striati (*Col.*) is well developed on the right.

Section 98 (fig. 15, Weigert; and fig. 16, Nissl) shows the radiation of the olfactory medulla forming the anterior part of the anterior commissure. An increasing number of medullated fibres is seen in the right internal capsule; they apparently radiate from the well preserved striatum and also from the posterior part of the gyrus orbitalis, which is also preserved. The striatum is bordered by a line of necrosis on both sides. The ganglia olfactoria Luysii are well developed. The septum and the striata contain old organized tissue and fresh hæmorrhages, the latter apparently due to mechanical irritation during the electrical stimulation. There is a symmetrical nucleus situated in the radiatio olfactoria medialis on both sides which is not mentioned in Winkler and Potter's "Atlas," but can be found in the normal cat series which has been used for comparison (fig. 16). Above the right nucleus, on the velum medullæ, are a few spots of indian ink, representing " Point 2 " (see fig. 15, " 2 "), Stimulation of this point gave rise to urination and changes in the respiratory rhythm.

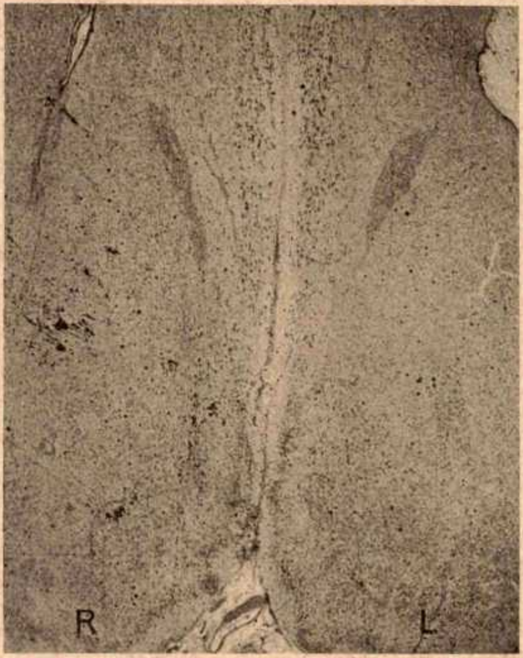

FIG. 16.

Section 113 (fig. 17) shows a considerable increase in the radiatio striothalamica (*R. Str. th.*), in the right internal capsule and in the anterior commissure (*Ant. comm.*) on both sides. On the left side, where the caudate (*N. caud.*) is less well preserved, a bundle of the radiatio striothalamica appears. The gyri fornicati (*G. forn.*) and corpus callosum (*Corp. Call.*) are seen above, and below the fibræ rhinencephales mammillares (*F.R.M.*) and the tractus olfactorius (*Tr. olf.*). On the extreme right is the gyrus Sylvius anterior (*G. Sylv. ant.*).

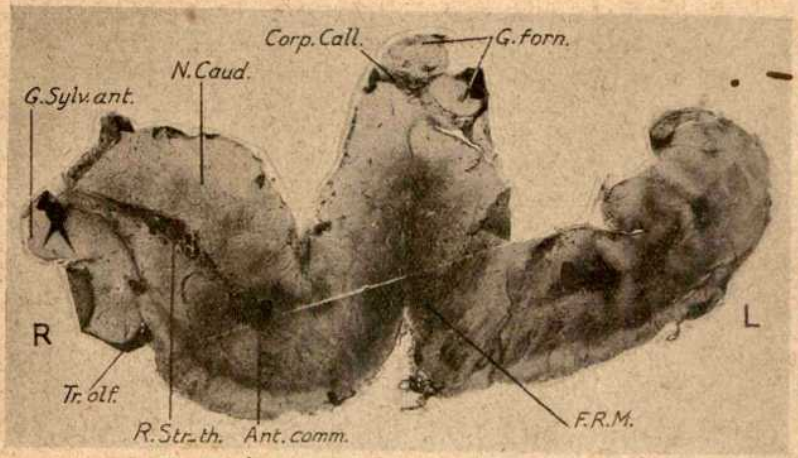

FIG. 17.

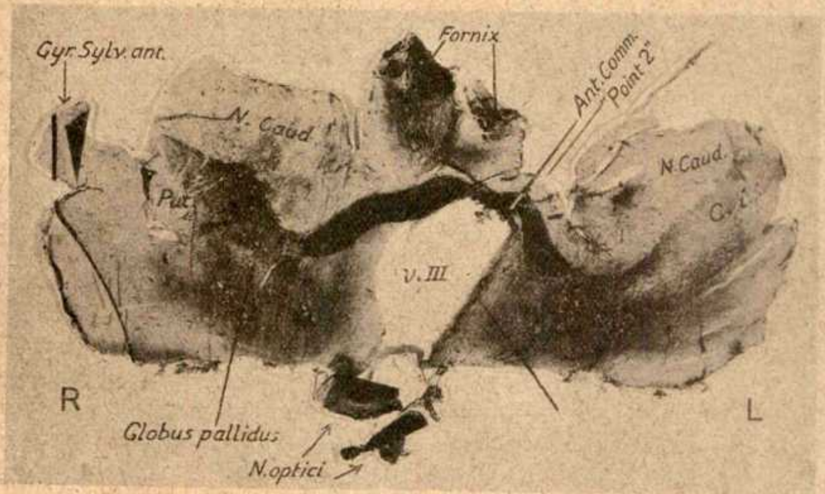

FIG. 18.

Sections 119 to 137 contain the well-developed anterior commissure. In all these sections some indian ink can be seen on the floor of the left ventricle just above the anterior commissure; it corresponds to "Point 2," from which licking and swallowing movements, puckering of the nose and epileptic attacks could be obtained by a faradic stimulation.

In section 134 (fig. 18, Weigert) the anterior commissure divides the specimen into an upper and a lower part. The upper part consists of the anterior end of the fornix, which still contains some fibres, and the caudate nuclei. Laterally the internal capsule (*C. i.*) joins the anterior commissure. Below the anterior commissure there is a large open space, the hydrocephalic third ventricle (*V. III.*) The globus pallidus and the anterior end of the nucleus amygdalæ can be seen. As in all sections, the right hemisphere is better preserved than the left and still contains the tractus olfactorius and a small portion of gyrus Sylvius anterior (*Gyr. Sylv. ant.*), both of which are absent on the left side. The optic nerves appear at the base (*N. optici.*).

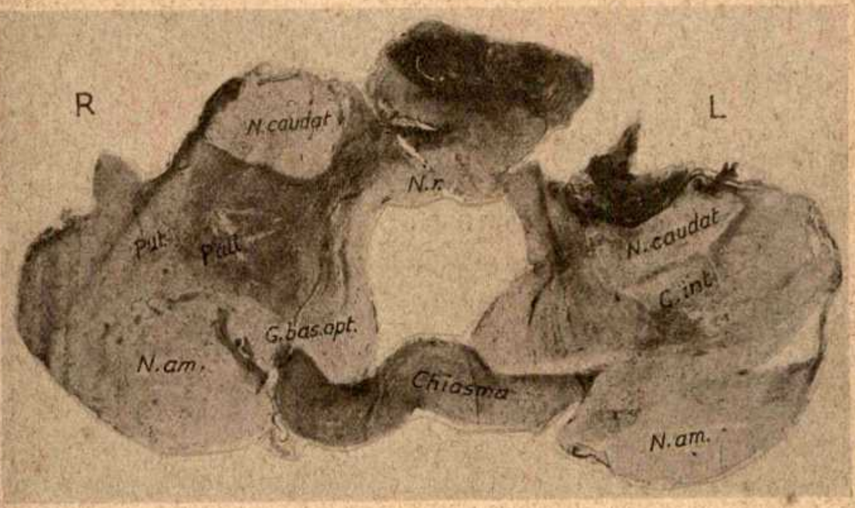

FIG. 19.

In sections 137-143 the choroid plexus is seen above the fornix. No part of the gyrus fornicatus remains. Below the anterior commissure the prethalamic nuclei can be seen; the nucleus filiformis is almost completely degenerated on the right side but is well preserved on the left. The contrast is especially marked in section 143. The first cells of the ganglion basale opticum appear.

Section 158 (fig. 19, Weigert) shows the nuclei caudati very well, especially in the Weigert preparations. The left nucleus is collapsed and has assumed a semilunar appearance owing to the deformation of the hemisphere. The ganglion habenulæ can be recognized. The chiasma is cut across and the optic tract enters the brain on both sides. The lateral and medial nuclei of the thalami are atrophic, but this is more evident in more posterior sections. The left thalamus is affected more severely than the right. On the right side the claustrum, nucleus amygdalæ, putamen and pallidum can be recognized; on the left side the putamen is deformed and the claustrum is absent. On the right side the cortex includes the frontal end of the gyrus Sylvius posterior and a small part of gyrus Sylvius anterior; on the left side only a part of the lobus piriformis remains. The medullated fibres on the upper surface of the temporal lobe belong to the stria terminalis.

Section 180 contains the pituitary gland and the anterior part of the degenerated left lateral geniculate body. The thalami are united by the massa intermedia. The fasciculus fornicis and the bundle of Vicq d'Azyr can be seen on both sides. The nucleus reuniens still contains a number of cells, and a few groups of cells remain which might correspond to *Mc* and *Va*. The nuclei filiformes are equally developed on the two sides.

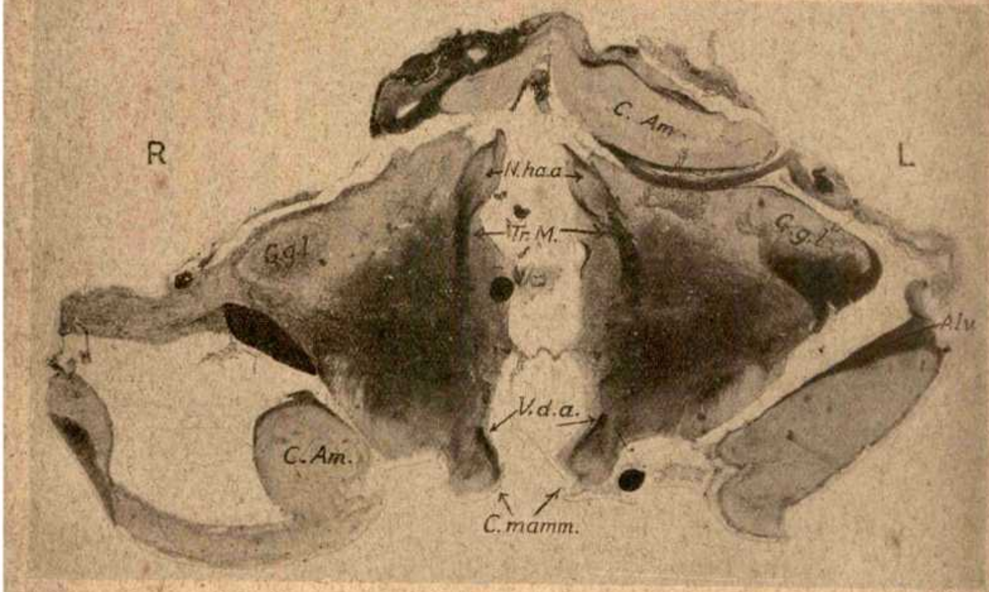

FIG. 20.

Section 193. The thalami are separated again, the right is better preserved than the left. The anterior end of each cornu Ammonis appears, and the left optic tract enters the lateral geniculate body. The posterior horns of the ventricles are very hydrocephalic, and that of the left is open laterally.

Section 206 (fig. 20) shows Meynert's tracts descending towards the base of the brain. The fasciculi of Vicq d'Azyr (*V.d.a.*) enters the mammillary bodies. The pyramidal tracts are completely degenerated in the pedunculi cerebri. The fibres of the substantia nigra and the other parts of the hypothalamus are well preserved. The left corpus geniculatum medialis can be recognized. The left fimbria is present, and the alveus (*Alv.*) is visible in each cornu Ammonis (*C.Am*). Only a few cells remain in the lateral geniculate body.

(*G.g.l.*). The nucleus parependymalis is well developed on both sides. The rest of the thalamus is degenerated and contains only a few cells, most of them grouped around Meynert's tract.

Sections 215-224 cut across the aqueduct of Sylvius and the anterior end of the posterior commissure. The optic tract enters the lateral geniculate body on the right side. The fibres of the pedunculus corporis mammillaris can be recognized. The pulvinar and the nucleus posterior thalami are completely degenerated.

Section 222 (fig. 21) shows the extent of the cortex which has been preserved; with the exception of the cornu Ammonis only the lobus piriformis remains. The structure of the different cell layers is the same on both sides.

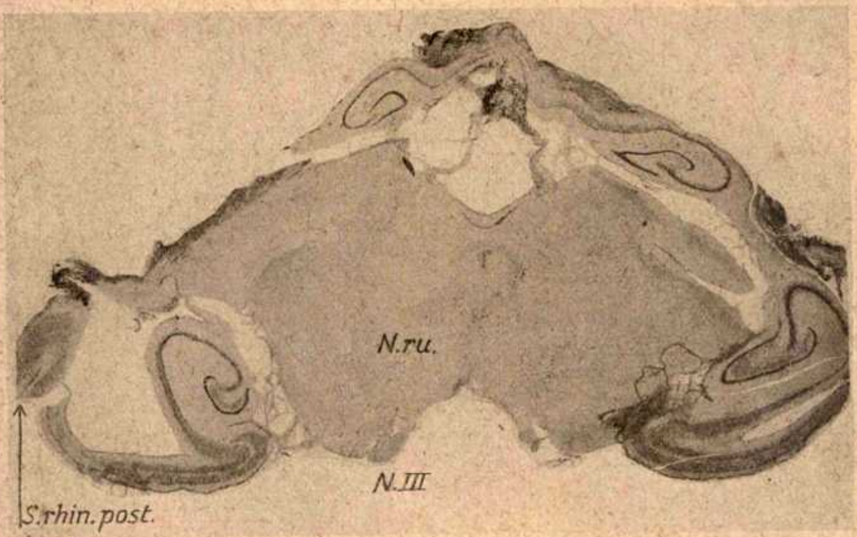

FIG. 21.

On the left side the cortex ends approximately between fields 28 and 35 (see Winkler and Potter). On the right side a part of the gyrus Sylvius posterior, containing part of area 35, is preserved. The third nerve (*N. III*) is cut across. The lateral geniculate body contains only glia. The medial geniculate body can now be recognized on both sides, but it contains only a few scattered cells. The optic radiations are completely degenerated. A good many cells remain in the region of the nucleus posterior thalami and in the pulvinar. The groups of cells around Meynert's tracts are well preserved. In section 224, Meynert's tracts are seen between the oculomotor nerves (see fig. 22).

In section 235 the red nucleus (*N. ru.*) and the substantia nigra appear normal. The medial geniculate body has disappeared on both sides. The brachium of the right posterior quadrigeminal body is severely degenerated. Neither peduncle contains medullated fibres, and the left is shrunken more than

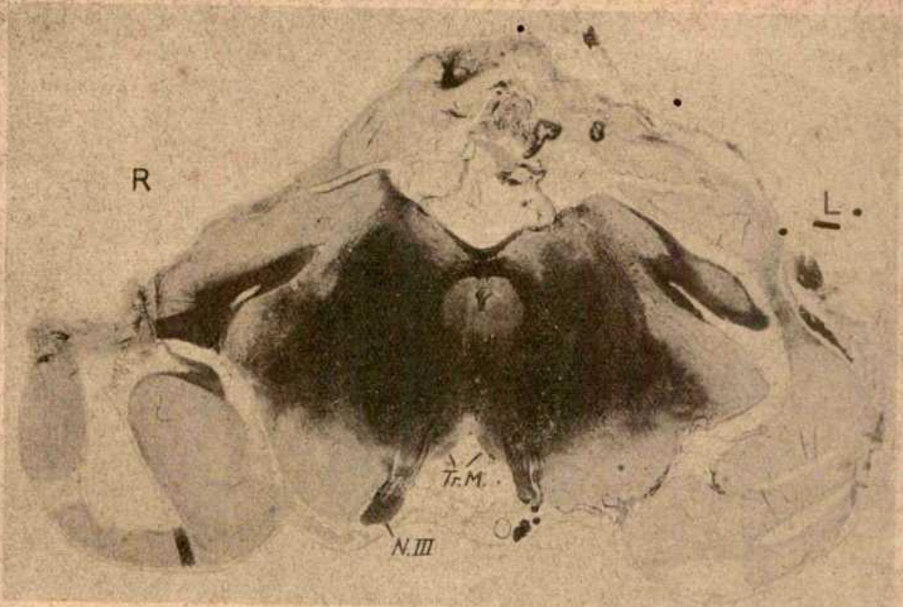

FIG. 22.

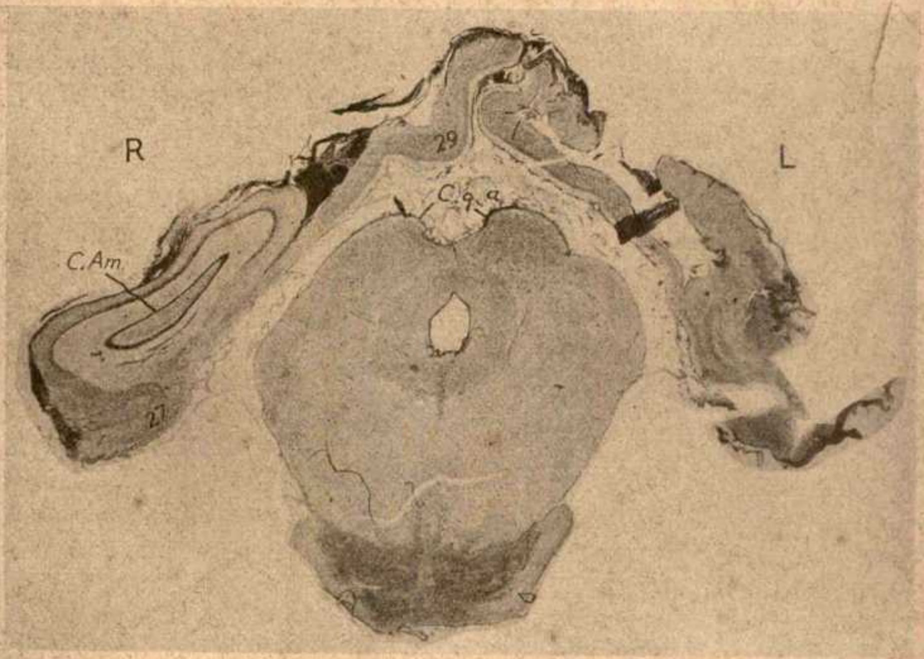

FIG. 23.

the right. Each cornu Ammonis contains a thin layer of medullated fibre. The lobus piriformis is still preserved.

Section 264 (fig. 23, Nissl) shows more cortex than the previous ones. The area 29 of the gyrus fornicatus is well preserved on both sides; some necrotic tissue from the adjoining areas is visible on top of it on the left side.

In Section 273 the chief abnormal feature is the degeneration of the brachium of the right posterior quadrigeminal body which seems to be due to a small area of necrosis in the lateral aspect of the quadrigeminal body. This necrosis can be recognized still better in section 286.

Section 278 shows even more cortex preserved. On the left side is the sulcus splenialis, a small piece of the gyrus splenialis posterior and the gyrus splenialis. The cortex covering this is not of the structure of area 17, but from its position must correspond to it. No medullated fibres remain in this region.

In sections across the pons and the medulla the pyramidal tracts are completely degenerated.

Summary of the Anatomical Findings.

More of the right side of the brain remained than of the left. Small portions of the convolutions which border the rhinencephalon were preserved on the right side, while on the left the operative incision followed almost exactly the sulcus præsylvius, the sulcus rhinicus anterior and the sulcus rhinicus posterior, so that even the lobus piriformis was removed and the olfactory tract was damaged. The subcortical ganglia were well preserved on the right side, but on the left the head of the caudate nucleus and the putamen were injured, and the claustrum was almost completely destroyed. The nucleus amygdalæ was intact on the right, and a considerable part of it remained on the left.

Some of the neocortex was preserved, chiefly in the frontal lobes. On both sides the gyrus proreus, the gyrus genualis and parts of the gyrus sigmoideus anterior and gyrus præsylvius remained. The anatomical examination showed, however, that with the exception of the gyrus proreus and gyrus genualis this neocortex must have been functionless, as its medullary layer was necrotic and the operative incision passed so far frontally that all the pyramidal fibres running around the ventricle were destroyed. On following the serial sections backwards the neocortex rapidly diminished, and when the genu of the corpus callosum was reached only a small piece of the gyrus rostralis was left. The genu, which is the only part of the corpus callosum which remained, was necrotic.

It is interesting that there were a number of myelinated fibres in each internal capsule, especially in the right. The study of the serial sections shows that these fibres were extrapyramidal, connecting the head of the caudate nucleus and the putamen with the lower parts of the basal ganglia. They correspond to the well-known radiatio striothalamica described by Rothmann [16], Dresel and Rothmann, Brouwer [4], Ferraro [7], and Karplus and Kreidl [9] in their decorticated animals. A small number of fibres in the right internal capsule may represent a radiation from the edge of neocortex which remained along the right rhinencephalon. That the internal capsule contained no pyramidal fibres was evident from examination of the mesencephalon, as here both peduncles are completely degenerated.

A good deal of cortex remained in the occipital poles. Area 29 (gyrus splenialis posterior) was well preserved, and small portions of the neighbouring cortex (areas 17 and 18) persisted on the left side, but they had lost their typical structure. Area 29 was probably functional as it was connected with the still medullated alveus. A study of the serial sections shows complete absence of the optic radiations, so the small remnant of the visual area (areas 17 and 18) cannot have had any fibre connections with the lateral geniculate body.

In places the injury was asymmetrical: for instance, the left nucleus filiformis was degenerated, while the right was well preserved. As the third ventricle was opened widely during the second operation, it is not impossible that this nucleus was damaged mechanically. A similar lesion to the right posterior quadrigeminal body probably explains the degeneration of the right posterior brachium.

While the hypothalamus seemed to be in a good state of preservation, the thalamus had undergone severe degeneration. The study of this series of sections confirms fully the findings of v. Monakow [14], Nissl [15], Brouwer [4], and others. The anterior and lateral parts of the thalamus were most severely affected, only the nucleus reuniens, the nucleus habenulæ, the nucleus parependymalis and the tract of Meynert escaped. The medial parts of each thalamus were better preserved. Only a few scattered cells remained in the nucleus centralis, nucleus posterior and in the pulvinar. The degeneration of the medial parts of the thalami was about the same on the two sides. The nucleus filiformis had disappeared on the side where the striatum was best preserved. The ganglion geniculatum laterale was also degenerated and contained only a few cells near the entrance of the optic tract.

The great majority of the cells of the ganglion geniculatum mediale had disappeared.

It is important that the thalamus was better preserved on the side where the striatum was intact. This indicates that some of its cells are connected with the striatum, though most of them are connected with the cortex.

Two of the points which were stimulated electrically could be located as they were marked with indian ink. On the left side "Point 2" lay on the anterior commissure. On the right side "Point 2" lay on the velum medullare anterior, above a comma-shaped nucleus of small cells which is found also in a normal cat.

SUMMARY OF PHYSIOLOGICAL OBSERVATIONS.

A review of the protocol of the animal "Kleopatra" shows that she possessed all the functions described by other observers in animals after removal of the forebrain, and in addition other functions not previously described. These were:—

(1) The elaborate mechanism which cats employ to keep their fur in good condition.

(2) A shaking reflex of the extremities, which was especially active during the first days after operation. These shaking movements could be regularly elicited by putting the paws into some sticky solution; immediately after the operation, though the limbs were weak, this reflex was so active that it developed spontaneously as soon as the animal placed her feet to the floor. This observation suggests that there was something in common between the movements of the partially paralysed limbs and the movement of a limb soiled with a sticky fluid.

(3) A state of hyperexcitability. This decorticated animal, in which the striatum was almost intact, was in a peculiar restless state for a prolonged period, especially when she was irritated by intercurrent infections.

(4) Polydipsia, polyuria and polyphagia immediately after the second operation. The only anatomical finding which can be brought into relation with this observation is the almost complete degeneration of the nucleus filiformis in the wall of the third ventricle on the left side.

A comparison of the electrical stimulation experiments with the anatomical findings gives two new results:—

(1) The production of smelling, licking and swallowing movements, and of epileptiform fits, by stimulation of the anterior commissure.

(2) Evacuation of the bladder and a change in respiratory rhythm on stimulation of the septum medullare anterior in the region of a comma-shaped nucleus. This nucleus consists of small cells; it is found in normal cats, but does not appear to have been previously described.

The other results of stimulation were indefinite and varied so much that it is difficult to attribute any value to them. The two positive results are conclusive, for we used bipolar stimulation, the reactions were very sharply localized, and the previous operations had produced complete degeneration of the radiations from the frontal neocortex.

A comparison of the behaviour of the thalamus cat and the striatal cat is not entirely satisfactory, because the thalamus cat lived for such a short time. It points, however, to the conclusion which has already been drawn by Dresel and Rothmann [16] that striatal animals have a wider range of motor activity and greater variation of behaviour than thalamic animals. The thalamus cat with its permanent, dull circus movements gave the impression of an automaton, while the striatal cat, even a few days after the operation, displayed a much greater variety of speed, direction and modification of gait, and responded more readily to auditory and sensory stimuli.

SUMMARY.

Two cats without neocortex are described clinically and anatomically. In the first both cerebral hemispheres were removed anterior to the thalamus; this animal lived for nine days after the second operation. It exhibited states of waking and sleep, and when awake it made purposeless circus movements. It did not eat spontaneously.

In the other animal the rhinencephalon and striatum were left intact; this animal was kept alive for five months after the second operation. Immediately after the second operation it showed much more activity and a greater variety of movements and of reactivity than the thalamus cat. It reached and ate its food spontaneously, and for a time it had polydypsia, polyphagia and polyuria, which were probably due to destruction of the right nucleus filiformis. Immediately after the operation the animal developed a well-marked shaking reflex of the extremities; this was shown to be an exaggeration of the normal shaking reflex which serves to clean or dry the paws. The animal cleaned its fur spontaneously. Its motor activity, when recorded in an "activity

cage," was found to be much greater than that of a normal cat. This excessive activity was excited by noise, and increased during infection by nematodes and mange.

Rotational nystagmus and after-nystagmus were studied on a rotating wheel, and were shown to follow the same rules as in intact animals and in man. As long as the speed and the amount of rotation were kept within physiological limits, the number of jerks depended chiefly on the degree of rotation. On longer rotation the after-nystagmus assumed the characters of a reaction to acceleration.

Electrical stimulation, immediately before the animal was killed, of those portions of the brain which remained revealed two points which were definitely excitable. The first proved to be the anterior commissure; stimulation of this produced movements relating to smelling and eating, as puckering of the nose, licking, moving the whiskers and chewing. The second point lay above a small comma-shaped nucleus in the velum medullare; stimulation of it gave rise to urination and changes in the respiratory rhythm.

The anatomical examination showed that, on the whole, the aim of the operations had been attained; the few portions of the neocortex which had been left had no fibre connections with the brain-stem.

The anterior and lateral parts of the thalami had undergone severe atrophy. This atrophy was more marked on the left side on which the striatum had been damaged.

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INTRACRANIAL ANEURYSMS.

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CASES of intracerebral aneurysms diagnosed during life must still be regarded as rare, although investigators recently have succeeded in diagnosing leaking or ruptured aneurysms in many cases. It is therefore worth while to see whether on a somewhat larger material diagnosis during life is as impossible as previous investigators (Gull, Beadles, Fearnsides, Wichern, among many others) have indicated. The difficulty appears to have lain in great measure in the fact that the possibility of aneurysm (Wichern) had not been thought of and that the different pictures of the disease were but little known. Intracranial aneurysm is certainly not a common disease, but on the other hand it is not a very infrequent one. In most cases aneurysms have a bad prognosis, especially when once they have begun to bleed, but on the other hand the possibility of effective surgical therapy, once the diagnosis is fairly sure, cannot be altogether excluded. It is therefore tempting to take up the question on a broader basis, especially since a number of questions concerning the ætiology, the pathogeny and the special pathological anatomy of intracranial aneurysms are still far from being answered.

Some case reports of intracranial aneurysms which have shown characteristic pictures by radiograms have appeared recently. These cases, to which I can add a new one, seem to open new diagnostic possibilities.

Having had occasion to observe personally some cases of aneurysm (one of these was diagnosed), I collected from the Department for Nervous and Mental Diseases of the Kommunehospital all the cases in which intracranial aneurysms had been proved by autopsy in the period from 1914 to 1929, both years included. As this material was not primarily examined with a view to scientific publication, it naturally has defects both on clinical and pathologico-anatomical grounds. The histories are often rather summary, as some of the patients were admitted in a state of coma, and death occurred shortly after. When an autopsy was made aneurysms were not specially sought for, and small aneurysms the size of a mustard grain or even larger may well have been overlooked. Only a few cases which gave no signs of aneurysm during life were found, because autopsies from the other departments of the hospital did not include the skull and brain unless symptoms of intracranial disease had been present. In several cases autopsy was forbidden by the relatives of the patient. The twenty-three aneurysms collected within fifteen years do not therefore express the real frequency of aneurysms. Further, all cases where death did not occur must be deducted, i.e., the cases discharged from the department.

HISTORICAL.

The first known description of intracranial aneurysms originates from Biumi in Milan in 1765. In the year 1834 Nebel reported thirteen cases, and Stumpf fifteen cases in 1836. In 1852 Brinton was able to report forty-nine cases (cited by Fearnsides). Gull in 1859 gave a description of the symptomatology of intracranial aneurysms, and has concluded that: "Although we may from the circumstances sometimes suspect the presence of aneurysms within the cranium, we have at best no symptoms upon which to ground more than a probable diagnosis." Gouguenheim, Lebert, Church, Bartholow, Ponfick, Peacock, Eppinger, Newton Pitt, Gowers, von Hoffmann, Simmonds and others have in later essays, some of which are classic, further widened our knowledge of intracranial aneurysms. In 1907 Beadles was able to report 555 cases, where intracranial aneurysms were found post-mortem, including 114 cases not published before; he too regarded it as quite impossible to diagnose an intracranial aneurysm, except in very rare cases: "I will go further and say that, in the vast majority of cases of aneurysms, tumour even cannot be diagnosed." Wichern (1911) was the first who emphasized the possibility of diagnosing this disease, because fifteen of his twenty-two cases in one way or another had symptoms of previous bleeding before the fatal one. Owing to the position which lumbar puncture had acquired in the preceding dozen years in the neurological clinic, where it was used as a common method of examination, a knowledge of the symptoms of subarachnoid hæmorrhage was established, especially its frequency (G. E. Schroeder), and it became possible to diagnose a ruptured or bleeding aneurysm. Later works of

Fearnsides (1916), Symonds (1923), Borchardt (1925), Parker (1926), and others gave a clearer basis for this diagnosis, particularly as it was shown how often an aneurysm gives rise to hæmorrhage, often several times, before the fatal severe bleeding takes place; a fact which corresponded well with the intermittent picture of the disease. Meanwhile it must be said to be still difficult to distinguish the bleeding of an intracranial aneurysm from other forms of subarachnoid hæmorrhage.

FREQUENCY, AGE INCIDENCE AND POSITION.

Before discussing the clinical picture of the disease in more detail, it is necessary to mention the frequency of cerebral aneurysms, their localization, and their relationship to age. Seeing that the smaller aneurysms are frequently overlooked at the post-mortem, it is by no means an uncommon disease. The frequency is diversely stated because of differences in material and technique of examination. The more minute the examination of the arteries of the brain the smaller the aneurysms one will be able to find, and aneurysms which have caused no symptoms during life will more frequently be an accidental discovery at autopsy.

They appear in about one-half to one, or one and a half per cent. of all post-mortems, though sometimes the frequency is stated to be less. Fearnsides found (in 1916) 44 cases out of 5,432 autopsies in all; Osler had previously found aneurysms in 12 cases out of 800 autopsies (cited by Fernsides). Newton Pitt had in the years 1869-1889 only found 23 cases out of 9,000 autopsies. On going through the records of 6,232 autopsies in which intracranial aneurysms were not suspected, Conway found this disease described in 43 cases. Busse had meanwhile by careful examination found in not less than 39 cases out of about 400 autopsies, aneurysmal formations on the anterior communicating artery. According to the statements of Bradford and Turnbull aneurysms are more frequent on the arteries of the brain than on those of the body, whereas the statistics of Crisp (cited by Osler) only show 7 intracranial aneurysms out of 501 cases of aneurysm, whereof 137 were on the popliteal artery.

In the above statistics, as in the following, only genuine aneurysms, or evident saccular or spindle-shaped limited dilatations, are included, while wide or doubtful dilatations of an artery are as a rule omitted. In my material only aneurysms from the size of a pea and larger are to be found. Furthermore, the arteriovenous aneurysms on the internal carotid artery in its course through the cavernous sinus have been omitted, as, because of the characteristic picture of this disease (pulsating exophthalmos) they naturally form an independent clinical entity (a classic work by Slomann and a new one by H. Ehlers on this subject are to be found in Danish literature). Furthermore, the multiple miliary aneurysms on the smallest branches of arteries which Charcot and Bouchard postulated as a frequent cause of cerebral hæmorrhage have been omitted, since their existence and signification are rather disputed, and they do not fall into the category of real aneurysms (Pick).

The true, larger intracranial aneurysms are almost exclusively localized on the greater extracerebral arteries, most of all on the arteries on the base of the brain near, or forming part of, the circle of Willis. Aneurysms are seldom found in the brain substance (but note my Case 17) or on the convexity of the brain (Reinhardt). The frequency with which the different vessels are attacked is rather differently reported, since with small series of cases accidental variations play a part. The place of predilection for an aneurysm is a bifurcation of one of the great arteries, or the place where smaller branches arise (specially the origin of a communicating artery), because these places anatomically represent the most delicate parts of the wall of the artery (Busse). According to Gowers (1893) they are most frequently to be found on the middle cerebral artery and thereafter with decreasing frequency on the basilar artery, the internal carotid artery, the anterior cerebral artery, the posterior communicating artery, the anterior communicating artery, the vertebral artery, the posterior cerebral artery, and the inferior cerebellar artery. Von Hoffmann (1894) stated the order to be: middle cerebral artery, internal carotid artery, anterior communicating artery, basilar artery, vertebral artery, anterior cerebral artery. The frequency of aneurysms on the basilar artery is very variously computed. Lebert regards them as rare, while von Hoffmann finds them rather often. They are frequently found in my material owing perhaps to the fact that it covers an extraordinary large number of cases of arterio-sclerotic aneurysms, as these tend especially to be located on the large vessels, while the embolic ("mycotic aneurysms," Eppinger) are most frequently found in the smaller vessels.

The 23 aneurysms in my material are grouped in the following way: the middle cerebral (the Sylvian fissure artery) 7 cases, the internal carotid 7 cases, the basilar artery 5 cases, the anterior cerebral 2 cases, the posterior communicating artery 2 cases, the ophthalmic 2 cases, the anterior communicating artery 1 case; in total 26 aneurysms in 23 individuals, as in one case 2 aneurysms were found, and in another case 3, in the same patient. In one case multiple dilatations of very arteriosclerotic cerebral arteries were found in the middle line; 8 aneurysms lay on the right side and 13 on the left. Bradford too found aneurysms more frequent on the left side. Wichern found the aneurysms on the middle cerebral artery more often on the left side. Ebert asserts the same with regard to the internal carotid artery and the posterior communicating artery. This has been explained by the fact that the carotid artery on the left side arises directly from the aorta. Yet Kerpola finds the aneurysms most frequently on the right side.

The incidence in the two sexes is also differently stated; according to Lebert women are more frequently the sufferers, but Hoffmann men. In my material are found seventeen women but only six men. The incidence too is differently stated; intracranial aneurysms are especially to be found between 30 and 60 years of age (Lebert, Krey), but they may be found at all ages.

In Wichern's series only seventy-one cases out of seventy-five were under 30, and only four were more than 60 years old; of the thirty-nine cases by Busse ten had not reached 40 years. The cases in my material vary from 11 to 75 years, whereof only three were under 30 years, while ten patients were over 30 and three over 70. In two cases the age is not known. Intracranial aneurysms thus most frequently give symptoms or involve death in the more advanced age periods, but they may occur in younger patients.

The size of the aneurysms vary from those which can just be seen, about the size of a mustard grain, to the size of a fist (Reinhardt), which no doubt is the largest intracranial aneurysm described. While some authors (e.g., Busse) report rather small aneurysms only found by systematic investigation of the arteries, other authors describe aneurysms of a larger size, e.g., when older post-mortem cases are recorded, as in this work. In my series no aneurysm smaller than a pea was included, two were as large as a plum (*vide* fig. 3), while one was of almost the size of a chicken-egg (previously published as a case report by Harald Møller in 1920).

There does not seem to be any connection between the size of the aneurysms and the localization in the different arteries (*vide* table) and it is more the ætiological factor, age and the like, which play their part here. Thus in Fearnsides' series of thirty-four arteriosclerotic aneurysms twelve were of the size of a pea and nine of them even smaller, while only six were over 6 mm. in diameter, the largest 30 mm ;

of thirteen embolic aneurysms three were of the size of a pea and none smaller, the largest was 25 mm. in diameter.

	The middle cerebral artery	The internal carotid artery	The basilar artery	The anterior cerebral artery	The posterior cerebral artery	The ophthalmic artery	The anterior communicating artery	
Size of a pea	2		1	1	1		1	6
Size of a cherry-stone	1							1
Size of a nut kernel		1						1
Size of a hazel-nut		2						2
Size of a cherry		1	1	1				3
Size of a shell-almond			2					2
Size of a walnut	2							2
Size of a plum		1				1		2
Size of a chicken-egg		1						1
Size of an index			1					1
No statement of size	2	1			1	1		5
Total	7	7	5	2	2	2	1	26

The ætiology is rather differently stated. In newer works congenital anomalies, local diseases in the wall of the artery due to septic emboli in ulcerative endocarditis, sepsis, pyæmia, universal diseases of the arteries such as arteriosclerosis, as well as traumata, are regarded as the most essential factors, whilst syphilis is unimportant. This will be dealt with later on. Arterial hypertension often co-operates with other factors in causing the bursting of the aneurysm.

We do not know how long a large aneurysm may exist without giving symptoms, but judging from the aneurysms accidentally found at autopsy, which have not caused marked symptoms, an aneurysm can exist for many years. Cases where an aneurysm has given clinical symptoms during a series of years have also been reported. One case published by Souques had presented symptoms of cerebral tumour for fifty-five years before the patient committed suicide at the age of 65, but this is a rather exceptional case. Among my cases, one (No. 15) had had symptoms for at least thirty-two years and possibly even longer. Only in a few cases is it possible exactly to determine when an aneurysm is formed, and this in fact only in case of the septic-embolic aneurysms (Wichern); in the case of Foster Moore, the aneurysm seems to have developed in the course of twenty-four hours, as a sudden blindness on the one eye marked the moment at which it damaged the optic nerve. The aneurysm, which came into existence in the course of morbus cordis, was diagnosed during life and proved eight weeks later post mortem.

SYMPTOMATOLOGY.

Among the symptoms of intracranial aneurysms one has to distinguish sharply between the symptoms of the original disease such as arteriosclerosis, ulcerative endocarditis, sepsis, pyæmia, &c., and the symptomatology of the aneurysm itself. In regard to the mycotic aneurysms the demonstration of the original disease is of great significance in diagnosis, but in arteriosclerosis the symptoms of this disease will often mask those of the aneurysm and render diagnosis impossible, as in several of my cases. Among the special symptoms of aneurysm one again has to distinguish between: (1) symptoms of increased intracranial tension; (2) local and focal symptoms caused by pressure or destruction of the nerves of the brain or of the brain-tissue or by atrophy of the cranium, &c.; (3) and finally the symptoms of beginning leakage or developed rupture, i.e., subarachnoid hæmorrhage. Further, a single symptom (intracranial bruit) has been considered as specific for aneurysm.

Symptoms of intracranial hypertension are seldom found in cases of aneurysm. Even in the case of Reinhardt where an aneurysm as big as a fist had caused considerable destruction of the bones of the cranium, there were no symptoms. In septic and syphilitic aneurysms it is very difficult to exclude meningitis as the cause of such intracranial hypertension. Fearnsides did not in any of his other cases find any symptom of this. In the very rare cases of optic neuritis due to aneurysms which are found in the literature, the cause was generally direct pressure of an aneurysm in the neighbourhood of the chiasma on one or both optic nerves and the consequent circulatory disturbances. In cases of bleeding from aneurysms symptoms of intracranial hypertension are very common, e.g., choked discs, although bleedings into the retinal tissue or the optic discs are often to be found and are rather characteristic. The cause is direct pressure on the optic nerve, perhaps from a clot, with impaired outlet from the central retinal vein (Goulden and Riddoch), or infiltration of blood down the sheath of the nerve (Dupuy-Dutemps). A frequent and characteristic symptom is headache, often severe and on the same side; it is as a rule caused by an incipient rupture.

The slow rate of growth and the very soft and yielding nature of aneurysms explain the above facts, and also the rarity of focal and local symptoms. It is not rare to find, for example, the optic nerve pushed forward and flattened, even imbedded in the wall of the aneurysm, without perceptible reduction of sight (as in my Case 9). Beadles found in only sixteen, or 4 per cent., of his aneurysms any sign of tumour, and in twenty, or 7 per cent., symptoms which might suggest cerebral growths. These local symptoms largely depend on the position, size, quality (calcified or not), rate of growth, &c., of the aneurysm.

The clinical picture depends on the localization of the aneurysms, but common to all is the fact that they sooner or later cause a subarachnoid hæmorrhage. Repeated bleedings often occur at intervals of years, up to 20 years according to Fearnsides. Wichern found this in fifteen out of twenty-two cases, and Fearnsides in about 42 per cent. of his non-embolic aneurysms, but at the same time no less than ten out of forty-four patients were admitted with symptoms of bleeding which soon led to death, without there having previously been evidences of hæmorrhage.

Some authors (e.g., Borchardt) consider every subarachnoid hæmorrhage for which no other cause can be shown as due to bleeding from an aneurysm, at least if the symptoms are intermittent, or if earlier bleedings had occurred. Others, as Guillain, do not mention intracranial aneurysms as causing subarachnoid hæmorrhage. Comte on the other hand gives an instructive description of the pathology and symptoms of intracranial aneurysms.

If we exclude traumatic hæmorrhages in which the nature and force of the injury will always be the decisive factor, it is the symptomatic and so-called "spontaneous" subarachnoid hæmorrhages which are difficult to separate from aneurysmal bleedings. In several cases the subarachnoid hæmorrhage may be idiopathic, but certain forms of hæmorrhagic encephalitis or certain cases of epidemic encephalitis may, apart from the subarachnoid hæmorrhage, pass without symptoms, or with symptoms so "masked" that the diagnosis of the original disease is impossible.

It seems probable that a spontaneous subarachnoid hæmorrhage is in the great majority of cases caused by aneurysm. The investigations of Busse have shown that even small aneurysms may cause a fatal hæmorrhage, that small aneurysms are far more frequent than previously supposed (about 10 per cent. of autopsies) and that these aneurysms are only found by very careful investigation. Gull pointed out in 1859 how difficult it is, post-mortem, to find the aneurysm in a case of bleeding, where it is quite imbedded in blood-clot. As the examinations of Busse only comprise the anterior communicating artery, aneurysms may be supposed to occur even oftener than stated by him, as the largest aneurysms, even the congenital, are not often found in this situation.

There is, however, an essential difference between aneurysmal bleeding and the other forms of subarachnoid hæmorrhage in that the latter are often (or always?) of venous origin (S. Goldflam), originating from the pial veins or plexus, while bleeding from aneurysms is an arterial bleeding, though often somewhat modified by thrombosis within the aneurysm (Emil John). When rupture threatens, a new coagulum may be formed, and the picture of the disease takes an intermittent course, which should make it easier to diagnose. Although other forms of subarachnoid hæmorrhage may occur several times in the same person (Babinski and Jumentié) this is exceptional.

I am, therefore, inclined to suppose that by far the majority of and perhaps all the spontaneous subarachnoid hæmorrhages which result in death are due to aneurysms. I assume that bleeding during several days and nights with remittent symptoms is characteristic, although more rapid courses or even with sudden death may occur. Subarachnoid hæmorrhage occurring several times in the same person, or of a remittent type, is most probably due to an aneurysm. That the post-mortem performed in the ordinary way does not prove this does not exclude the presence of aneurysm.

When a young, previously healthy person is suddenly seized by symptoms of a subarachnoid hæmorrhage and no organic disease of the brain nor a considerable trauma can be shown to be its cause, one must always think of a burst aneurysm. The following cases are cited as examples of this:—

Case 1.—An unmarried woman, aged 23, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital, December 18, 1920, and died here December 21, 1920. She was always of a somewhat slender build, of delicate health, sickly, often tired; has had "anæmia," no inflammation of the lungs, no scrofula.

She was taken suddenly ill on December 13, and began to cry aloud on account of violent headache; she vomited the whole first night, not later. She was somewhat confused, remained in bed, took very little food. There was no convulsion or paralysis, but a fixed upward position of the eyes. No grinding of the teeth, stiffness of the neck, nor cry was noted. She dozed, spoke only a few words and complained of headache. Incontinence of urine occurred during the last day and night.

During her stay here, she was drowsy, slow, far-off and distracted, but conscious and knew where she was.

On examination.—She was of slender build. Stiffness of the neck and Kernig's sign were present, but no strabismus. The pupils were small and reacted. Knee-jerk, Achilles tendon and plantar reflexes were absent on both sides. Otherwise no neurological signs were noted. Rectal temperature was 38·5° C. on admission, and next morning 38·9° C. Pulse 76 and 80.

December 20, temperature 39·5° to 39·3° C., pulse 84 to 88. There was increasing drowsiness, possibly double vision and facial paresis on the right side, with stiffness of the neck and Kernig's sign. The tendon reflexes in the upper extremities were brisk but were absent in the lower extremities.

On ophthalmoscopic examination, optic neuritis was found in both eyes and in the left eye hæmorrhages near the disc.

Lumbar puncture gave a light yellow, blood-stained fluid which contained twenty-eight lymphocytes and larger mononuclear cells and about 300 red cells per cubic millimetre; globulin was absent, albumin 10 (Bisgaard). No bacilli were found and no growth was obtained on ascites-agar and bouillon.

On December 20 there was no definite paresis of the cranial nerves, but slight outward deviation of the right eye. Temperature unaltered, 39·7° C. Pulse 120.

On December 21 both optic discs were swollen, with exudates and hæmorrhages (optic neuritis). The condition otherwise was the same. She dozed, did not eat and died quietly with increasing hyperthermia.

Clinical diagnosis: Meningitis tubercolosa?

December 22 autopsy: On removing the brain abundant blood streamed out from the underside of the frontal lobe, where many clots were found. The blood came from a cavity the size of a plum in the lower side of this part the brain. In the middle line of the coagulum and to the left of it an aneurysm the size of a cherry was found on the anterior cerebral artery.

The brain was preserved and on section the hæmorrhage was shown to be situated between the brain and the pia mater, but it did not extend into the brain-tissue itself.

The post-mortem also revealed fibrous myocarditis and broncho-pneumonia in the right lower lobe.

The aneurysm was thought to be congenital (further details on p. 526).

The clinical picture of this case did not indicate more than the probability of an aneurysm.

The symptoms of such an aneurysmal bleeding are those of the subarachnoid hæmorrhage. The intense headache is very characteristic; it is violent, as a rule on both sides, at times of neuralgic form (trigeminal irritation), or accompanied by vomiting, dizziness or other cerebral (cortical) symptoms; the irritative symptoms as a rule obscure the inhibitory. Different clinical pictures include convulsive, hemiplegic, aphasic, meningeal, comatose or purely psychotic forms with mental confusion or hallucinations (Flatau).

The onset may be apoplectiform or more insidious. Before the final rupture sets in there may be symptoms of a menacing rupture, as in the following case :—

Case 2.—A man, aged 26, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital on December 29, 1916, and died within twenty-four hours.

It was learned that his family history was negative. From the information obtained from his fiancée, he had previously been healthy up to the last two or three weeks before admission. He then took to bed with violent pains in the extremities and a very severe constant headache with occasional exacerbations, associated with violent vomiting. There was no fever or disturbance of vision. He had not complained of dizziness before the morning of admission when he was getting up. At 2 p.m. he had an attack of convulsions in all limbs with biting of the tongue, but without incontinence. Since then he had been comatose, but at 3 p.m. he had another similar attack.

He was admitted here half an hour later, totally comatose and very exhausted. The respiration was deep and snoring, about 12 per minute, pulse 62, irregular and soft; rectal temperature 36·6° C. He did not move the right extremities, which were more flaccid than the left and showed increased tendon reflexes. A typical Babinski response was present on both sides. The pupils were slightly contracted, equal, and did not react. No strabismus or ptosis. The right corneal reflex was absent. The right angle of the mouth drooped. He incessantly ground his teeth. The tongue was bitten in several places. The chest was healthy, the heart sounds distant and low, with a somewhat irregular faint systolic murmur, which seemed to be loudest at the apex and at the pulmonary area. No dullness over the manubrium sterni was found. The abdominal reflexes were absent on the right side. Stiffness of the neck and Kernig's sign were not observed. The ears were normal. The ophthalmoscopic examination showed normal conditions, at least in the right eye.

The urine obtained by catheter contained albumin and sugar. A lumbar puncture gave bloody spinal fluid which ran out slowly. The Wassermann reaction of both blood and spinal fluid was negative.

He became feeble, flaccid and pale; the left pupil was larger than the right and neither reacted to light. He died suddenly two and a half hours after admission.

Clinical diagnosis: Subarachnoid and cerebral hæmorrhage; glycosuria.

Post-mortem · A large hæmorrhage in the third ventricle passing down into the fourth ventricle and the central canal was revealed; it originated from an aneurysm at the base of the right temporal lobe arising from the middle cerebral artery.

Except for a traction diverticulum in the œsophagus about 1 cm. deep, nothing abnormal, and especially no evidence of syphilis, was found.

The aneurysm was supposed to be congenital.

This case seems to be so typical that it undoubtedly could have been diagnosed. The picture of the impending rupture was especially characteristic and well pronounced. With reference to the differential diagnosis, it should be remembered that a severe degree of albuminuria occurs in subarachnoid hæmorrhage (G. Guillain, Cl. Vincent, Schneider, Symonds) but quickly disappears. Guillain considers a pronounced transitory albuminuria indicative of subarachnoid hæmorrhage, whereas slight albuminuria has no significance. It is probably due to central vasomotor disturbances. In my material the albuminuria was never intense, but transitory albuminuria occurred. The glycosuria, which is frequently seen, is supposed to be of central origin also. Guillain also considers a bilateral Babinski reflex as of certain significance in the diagnosis of subarachnoid hæmorrhage.

When the onset is apoplectiform the differential diagnosis will always be difficult as against a cerebral hæmorrhage, which secondarily bleeds into the subdural space or breaks into the ventricles. There is the added difficulty that a hemiplegia frequently occurs with these forms of subarachnoid hæmorrhage. If the hemiplegia proves to be severe and permanent, or if there is pronounced retraction of the head and deviation of the eyes, then a deeper injury of the brain is more probable (Guillain), but this also may be due to a ruptured aneurysm, as in the second of the two following cases.

Case 3.—A married workman, aged 70, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital, May 3, 1921, and died here May 5, 1921.

He had previously enjoyed good health and had never had similar attacks before. He had never been absent from his work during more than thirty years. He is said to have been injured immediately before his admission by falling over a rail, he fell flat on his face and immediately lost consciousness; according to an eye witness he walked with a reeling gait before he fell, then he stood still, swayed a moment and fell. After that he began vomiting.

On his admission to the hospital there was a hemiparesis on the right side with drooping of the right angle of the mouth. Next day he was in a state of coma and did not react; there seemed to be paresis of the right arm, but otherwise no focal symptoms. Babinski's sign was absent; the blood-pressure was 145 mm. Hg. The urine contained sugar. He died in a state of coma, without having regained consciousness, on the afternoon of May 5.

Clinical diagnosis: Hæmorrhagia (?) cerebri. Hemiplegia dextra.

Post-mortem: No fracture of the cranium was found, but very considerable subpial bleeding. This originated from a ruptured aneurysm, the size of a cherry, on the posterior wall of the left carotid artery, at the origin of the middle cerebral artery. The blood had reached both the Sylvian fissures, and the left Sylvian fissure especially was distended by blood. There was no bleeding into the brain tissue itself.

There was slight intimal proliferation, but no arteriosclerosis in the branches of the coronary arteries; diffuse intimal proliferation in the aorta, arteriosclerotic plaques in the descending aorta, and some arteriosclerosis in the abdominal aorta were present. Purulent bronchitis and bronchopneumonia were present on both sides as well as hypertrophy of the left ventricle of the heart. The aneurysm is supposed to be arteriosclerotic.

Case 4.—A man, aged 55, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital October 21, 1916, and died on October 22, 1916. He was brought in by ambulance after an attack of unconsciousness which occurred while he was at work. He was found on admission to be comatose and could not be made to react. All the reflexes, including the conjunctival, were abolished. The pupils were much contracted, the heart normal but its action somewhat irregular, the pulse 66, rather weak, the respiration quickened and groaning. Urine: albumin present, no sugar. Temperature 35·8° C. Later some vomiting and œdema of the lungs with blackish foam round the mouth developed. In the evening a Babinski response was obtained from both feet and the tendon reflexes were fairly brisk. Temperature 39·9° C. Next morning he was moribund, temperature 40° C. There was complete atony of all extremities, and the pupils were maximally contracted. He died quietly within twenty-four hours.

Post-mortem: No evidence of fracture of the cranium. Arteriosclerotic changes were seen in the vessels at the base of the brain. The left hemisphere was distended, and here a considerable hæmorrhage was found, which had destroyed the central ganglia and had broken into the ventricles, which it had distended with blood. On the surface of the brain subpial hæmorrhage was seen round the pons, medulla and cerebellum.

In the disintegrated central ganglia on the left side a more compact nodule was found; this turned out to be an aneurysm, the size of a cherry and full of coagula, on a small branch of the middle cerebral artery.

The heart was of normal size without special hypertrophy of the left ventricle; the valves were normal. The coronary arteries were slightly arteriosclerotic, as was also the abdominal aorta. Fatty degeneration of the liver and the remnants of old tuberculous lesions at the apices of both lungs were found, but no other gross changes. The aneurysm is supposed to be arteriosclerotic.

In the first case a lumbar puncture would have revealed the subarachnoid hæmorrhage; the absence of focal symptoms would have suggested a hæmorrhage from an arteriosclerotic extracerebral artery. In the last case the aneurysm could not be diagnosed.

The senile brain may react even to severe subdural hæmorrhage, as in the case below, in such a way as to give the clinical picture of a senile or arteriosclerotic confusion.

Case 5.—A woman, aged 72, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital, March 23, 1922, and died there April 2, 1922.

No information about similar previous attacks or other diseases was available. She was suddenly taken ill six days before admission, while alone at home, and was found six to ten hours later lying dressed on her bed, soiled with urine and fæces (unconscious?) She had remained in bed since and had been somewhat confused; the last two days and nights she had been very restless, running about on the floor and crying aloud.

When in hospital she was somewhat confused. She did not know where she was and wanted to get out of bed. Temperature 37·8° C. The pulse was 60, regular and strong. The peripheral arteries were rather hard and tortuous, the knee-jerks absent on both sides. On admission the Babinski response was present on the left side, later on both sides. She had to be catheterized. The urine contained albumin (slight). The blood-pressure was 100 to 165 mm. Hg. On March 24 she was more clear and collected, and fairly well oriented; no pareses nor disturbances of speech were noted. The catheter had to be used. On the following days she was rather somnolent. On March 28 she was more tranquil but not quite conscious. On the 29th lumbar puncture gave a diffusely blood-stained fluid, containing 146 cells and about 800 erythrocytes per cubic millimetre; globulin 1, albumin ·25. Wassermann reaction was positive in the blood, but negative in the spinal fluid.

Ophthalmoscopic examination showed senile cataract. She was by turns drowsy and very restless during the following days. On April 2, respiration became weaker and she died quietly in the evening.

The clinical diagnosis was encephalomalacia arteriosclerotica, ictus apoplecticus, confusio mentis.

Post-mortem examination: On opening the cranium an enormous hæmorrhage was seen which reached from the chiasma forward along the olfactory tract and round on to the convexity of both frontal lobes. It originated from a small ruptured aneurysm on the anterior communicating artery. In the brain-tissue itself there was no hæmorrhage.

Additional findings were an echinococcus-cyst in the liver, verrucose endocarditis on the valves of the aorta, universal arteriosclerosis and terminal bronchopneumonia. The aneurysm is supposed to be arteriosclerotic.

The motor phenomena may vary greatly. The hæmorrhage may spread along the vessels or under the pia on the cortex, or flat coagula may form over the hemispheres so that convulsions, perhaps of the Jacksonian type, or hypertonia and spasms of different kinds develop. In four of my cases convulsions occurred. A symptom often found in my cases was abolition of tendon reflexes of the lower extremities. In a few cases this was associated with a bilateral Babinski response. In some cases the increased tendon reflexes of hemiplegia became reduced when a loss of the deep reflexes of both the lower extremities appeared. This loss of tendon reflexes has been described by Guillain among others but is said to be fairly rare. In my material it occurred frequently, at least after the first two days. It may possibly be characteristic of larger (arterial) hæmorrhages. It has been found on several examinations (by different investigators) in most of my patients and must therefore be regarded as certain. It is also extraordinary when compared with the usually increased reflexes of the upper extremities. Sometimes the passage of blood may almost be followed over the surface of the brain and down into the spinal canal. As an example of motor symptoms of irritation the following case can be given.

Case 6.—A woman, age unknown, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital, April 30, 1914, and died there May 1, 1914.

She was admitted in a comatose state. No information was available She moved both her upper extremities occasionally. Slight reflexes were present on both sides. There was some rigidity of the flexors of the elbow joint on both sides, especially the right. The lower extremities were relaxed without reflexes. The pupils did not react to light. The right nasolabial furrow was absent.

A couple of hours later she was still comatose, the arms drawn up and bent at the elbow-joints, the hands clenched and from time to time convulsive movements of them occurred. Leri's reflexes were not present; a Babinski response was obtained on both sides; there was no deviation of eyes or retraction of the head. Cheyne-Stokes' respiration was noted She died during the night.

Clinical diagnosis: Apoplexia cerebri

Post-mortem: The surface of the brain was covered all over with coagula, especially round the right temporal lobe and in the anterior part of the longitudinal fissure, round the genu corporis callosi. The arteries were slightly arteriosclerotic. On the left anterior cerebral artery was found a ruptured aneurysm the size of a rather large pea with arteriosclerotic walls. No changes in the bones of the cranium were seen.

The heart was of normal size with normal valves. The coronary arteries were slightly arteriosclerotic. In the descending aorta arteriosclerotic changes with slight calcification and atheromatous plaques were seen.

The aneurysm is most probably arteriosclerotic, but in the absence of further history the diagnosis was impossible.

A bleeding aneurysm presents the same symptoms as other forms of subarachnoid hæmorrhage; they may be as variable and capricious. The materials for the diagnosis must be gathered from the special course of the hæmorrhage, the way it arises, possibly previous symptoms of impending rupture (headache, vomiting, radiating pains, transient paresis of the cranial nerves) and from the intermittent course of the whole disease. The diagnosis on this basis is far from sure, but a certain presumption is possible that it is a case of aneurysm with hæmorrhage, as in the last of the following three cases, in which the aneurysm was diagnosed during life.

Case 7.—A woman, aged 60, married, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital, July 29, 1918, and died on August 10, 1918.

She had been healthy for many years, and there had been no signs of kidney disease. An hour after she had gone to bed in the evening she began to moan in her sleep, was restless, querulous, holding her head. She did not respond when addressed; had "convulsions" during which she fought with both arms and legs, and violent vomiting, and was then admitted to the hospital. Here she was restless, crying "Oh my head," with constant vomiting. Fæces and urine were passed involuntarily; she did not respond when addressed. The right side of the face was smooth and drooping. Later she was stuperose. Next day her condition was unchanged. The pupils were now small and without reaction. Facial palsy was noted on the right side, and plantar reflexes of the Babinski type. The tendon reflexes were absent in both lower limbs She cleared mentally during the following day, and became more oriented. There was no asymmetry of the face, but a Babinski response was still present on the right side The urine contained sugar, no albumin. Blood-pressure: 180 mm. Hg systolic. On August 1, the urine contained albumin, no sugar. On August 3, she has conscious and knew where she was. She was allowed out of bed.

On August 4, the temperature was 38·8° C. Objectively nothing abnormal was found. On the following days fever and headache increased. On August 7 she was foolish and confused. with Babinski response on both sides. On August 10, ophthalmoscopic examination of the right eye was impossible, but the left eye showed choked disc. The urine contained albumin. She died the same evening. Lumbar puncture was not performed.

Clinical diagnosis: Coma, glycosuria, subarachnoid hæmorrhage.

Post-mortem: The vessels at the base of the brain were very sclerotic.

The right internal carotid artery was considerably enlarged, and this continued into the right middle cerebral artery, around which there was a considerable hæmorrhage. Similar but less pronounced hæmorrhage was found around the left middle cerebral artery. The hæmorrhage originated from a ruptured aneurysm, corresponding to the right posterior communicating artery, which could not be located. Corresponding to the place of the aneurysm a partly old and a partly new hæmorrhage was found, stretching down around the right optic tract and behind the corpora mammillaria. The subpial hæmorrhage stretched along the vessels right up on to the convexity of the brain.

Throughout the whole aorta very marked arteriosclerosis was seen, with pronounced calcification.

The left ventricle of the heart was hypertrophied. Calcified bronchial glands, a diverticulum of the œsophagus and an ovarian cyst on the left side were also found.

The aneurysm was arteriosclerotic in origin.

Case 8.—A married woman, aged 64, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital, December 29, 1926, and died on January 10, 1927.

At her place of work she was said lately to have had attacks of pallor, but they quickly disappeared. Otherwise she was always healthy.

She fell suddenly ill on the day of admission, and her husband found her unconscious on the floor. On admission here she was very restless, wanting to get out of bed, chattering, holding her head. She had obviously totally lost her bearings. She vomited at first and later was nauseated; she made no response when addressed. Objectively nothing abnormal was found. Blood-pressure 160/85 mm. Hg. The urine contained albumin (Esbach 1·5 per cent.).

She regained consciousness the next day, was more collected and was able to give some information, otherwise soporous. The following day she was fairly conscious, quiet, complaining of headache and some nausea. The left pupil was somewhat larger than the right. There was paralysis of the right sixth nerve, but no diplopia. Otherwise no neurological abnormalities and no Babinski response were noted. Lumbar puncture gave blood-stained spinal fluid. Pressure before the evacuation 180 mm. After the evacuation of 1½ cm. 520 mm. (?). On centrifugalizing the fluid was obviously yellowish, containing albumin 60, globulin 3, i.e., increase of albumin beyond the admixture of blood.

January 3. Ophthalmoscopic examination: maculæ and corneæ normal. Myopia progressiva. Choroidoretinitis.

January 5. No complaints, psychically normal. Paralysis of the sixth nerve diminishing.

January 10. In the morning she suddenly collapsed when dressing, and death occurred shortly after.

Clinical diagnosis: Subarachnoid hæmorrhage.

Post-mortem · Very considerable subarachnoid hæmorrhage especially round the pons and medulla oblongata. On the posterior communicating artery an arterial distension rather larger than the size of a pea was found filled with coagula.

The heart showed some hypertrophy of the left ventricle, and the whole heart was somewhat enlarged. The coronary arteries were rigid and tortuous with atheromatous thickenings. The aorta showed rather pronounced sclerotic changes from the arch downwards. Very broad atheromatous thickenings were present in the arch and, to a less degree, in the ascending aorta.

Further findings were myofibrosis cordis, stasis hepatis et renum, fibromata uteri and pelveo-peritonitis chronica.

Microscopic examination of the aneurysm showed no definite inflammatory changes in the wall, but at the point of its origin the intima was thickened The wall of the aneurysm consisted only of intima and a thin adventitia.

In another preparation a small vessel was seen with thickening of the intima, as well as arteritis of the media and adventitia. Infiltration of round cells was also seen at several places in the medulla oblongata and meninges round the cerebellum. There was extravasation of blood in and round the meninges.

It is likely that the aneurysm was of infectious origin, but its real nature could not be decided.

Case 9.—A widow, aged 49, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital, September 19, 1929, and died there September 28, 1929.

In the family of the father there were some cases of apoplexy. Except for otitis media as a child, with resultant deafness of the right ear, and uncomplicated diphtheria in her 28th year, she had always been healthy. The climacteric had begun, but menstruation had not yet altogether stopped.

She was brought to the hospital by the ambulance, having been immediately before found lying unconscious on the floor of the bathroom, where she was taking a warm bath. She had been all right before the bath. She did not respond when addressed, but responded briskly to the examination and to pricks with needles: she was restless, turning about in the bed, and preferred to rest on the left side. There was less movement of the extremities on the right side, at least of the right arm. They did, however, move actively in response to pricks. Tonus and reflexes were normal. A doubtful Babinski response was obtained on the right side. Both eyes were tightly closed, the right could be opened passively, the left not. The pupils reacted normally. The eyes were moved freely. The right angle of the mouth was slightly smoothed out.

Heart: Limits normal, no murmurs. The action very irregular with extrasystoles. Heart-beats 116, pulse 100. Blood-pressure 180/90 mm. Hg. No meningeal symptoms. The urine contained no pathological elements.

Next day her state was unaltered; she was restless, talking nonsense, confused, and did not know where she was. On sitting up in bed in the morning she suddenly fell back with rattling respiration, became quite pale, and passed urine involuntarily.

September 21. Still somewhat absent and slow, talking nonsense. No aphasia. No paralysis, eyes normal. Knee-jerk and Achilles-tendon reflexes weak, especially on the left side. Plantar reflexes absolutely normal. No meningeal symptoms.

September 22. Temperature yesterday evening 38·5° C., this morning 37·6° C. Tired and somewhat distraught, otherwise physically normal. Nothing was found which might explain the rise of temperature.

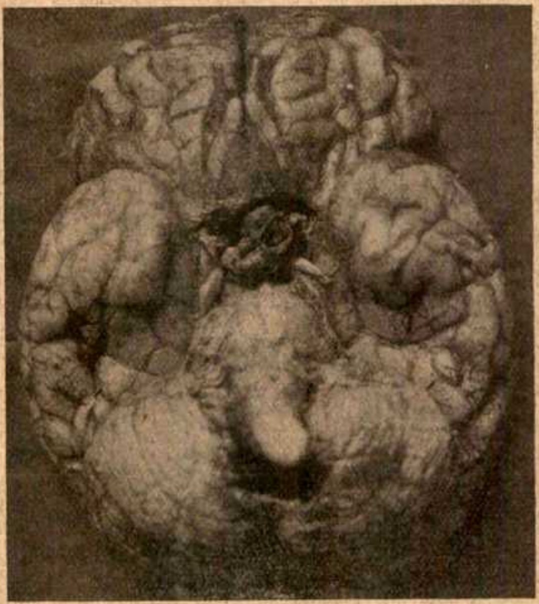

FIG. 1 (*Case* 9).—A ruptured aneurysm on the internal carotid artery in a woman 49 years of age.

September 23. 39° C. to 29·7° C. Yesterday afternoon there was severe headache. She was complaining, dozing or unconscious and had some stiffness of the neck.

Lumbar puncture: Spinal fluid blood-stained, identical in three portions. On centrifugalizing the fluid on top is slightly yellowish. It contains 31 cells and 13,000 erythrocytes. Globulin 1? albumin 14.[1] Probably slight increase of cells, no evident increase of albumin more than due to the admixture of blood. The Wassermann, Sigma and Kahn reactions of the blood and cerebrospinal fluid were negative.

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[1] Determined by the methods of Brandberg, Stolnikow, Ross, Jones and Bisgaard. In this paper, globulin refers to that part of the protein content of the spinal fluid which is precipitated by semi-saturation with ammonium sulphate. Albumin is the portion of protein which is precipitated by nitric acid as in Heller's test.

September 24. Increasing meningeal symptoms. Ophthalmoscopic examination: a couple of small hæmorrhages on the right optic disc and around the disc, otherwise normal.

Increasing meningeal symptoms and stupor.

September 26. Hemiplegia of the right side with motor aphasia. Right plantar reflex absent, left normal. Fixed position of the eyes upwards and to the left. Slight twitching in the muscles on left side. The patient died with increasing meningeal symptoms on September 28.

Clinical diagnosis: Aneurysma cerebri rupta.

Post-mortem: On removing the brain, a small amount of blood was found in the anterior fossa in the subdural space, together with some subpial hæmorrhage in front on the surface of the right frontal lobe, and a smaller compact hæmorrhage on the lower side of the cerebellum. The leptomeninges were hyperæmic. On the left internal carotid artery a thin-walled aneurysm, scarcely the size of a hazel-nut, was found; it compressed the left optic nerve, which was stretched over its anterior end. The aneurysm seemed to originate from the main stem, not from the communicating artery. It did not seem to be in connection with the cavernous sinus. It was not possible to determine the exact place of the rupture, but a small piece of the base of the aneurysm remained behind on the lateral edge of the sella when the brain was removed. On horizontal section through the brain, hæmorrhage was found in both the lateral ventricles. No signs of external violence of the cranium, and no signs of fracture were present.

The heart was normal, the coronary arteries slightly sclerotic, the aorta without dilatations and only slight atheromatous changes. Otherwise nothing abnormal, excepting hypostasis in both lungs, was discovered.

The microscopical examination of the aneurysm showed considerable thickening of the intima with atheromatous degeneration, and in several places layers of calcium. The media was thin, the elastica interna frayed.

Histological diagnosis: Aneurysm with atherosclerosis.

These three cases give rather characteristic pictures. The two first should at any rate have suggested a burst aneurysm, especially Case 8, in which the paralysis of the abducens pointed in the direction of an aneurysm on the posterior communicating artery. The fact that the diagnosis was considered possible in the last case is due to the characteristic cause of the bleeding (congestion by the warm bath) and the intermittent course of the disease. In Cases 7 and 9 the increase in the temperature was the first sign of a renewed bleeding, as it sometimes is (Zádor).

On the whole a rise of temperature is not rare, especially in more chronic cases; it is due either to direct central irritation or to absorption of the hæmorrhage. If such an increase of the temperature occurs together with torpor or stupor, and if the aneurysm at the same time causes paralysis of the ocular muscles (e.g., aneurysms on the posterior communicating artery) the differential diagnosis as against encephalitis is difficult, especially since one may, despite a large subarachnoid hæmorrhage, occasionally obtain normal spinal fluid by lumbar puncture. (Pierre Marie and Faure-Beaulieu, Barth and Cahen, Zádor.)

In twenty of my twenty-three cases aneurysms have been the cause of hæmorrhage and this hæmorrhage has been the direct cause of death. In some cases death occurred quickly; thus two persons died immediately on their arrival at the casualty room of the hospital (in one case there were, however, other causes of death), in other cases not until hours later or even after several days. How frequently hæmorrhages previous to the one which led to admission had occurred is not indicated in my material, as the histories are not exhaustive in all the cases. The process and symptomatology of this hæmorrhage have been illustrated by different examples. In the following case hæmorrhage occurred in association with acute miliary tuberculosis; unfortunately both the history of the disease and the objective examination of the patient are missing in this case.

Case 10.—A girl, aged 11, was admitted to the Department for Nervous and Mental Disease of the Kommunehospital, March 29, 1914, after four hours of convulsions at home and died on her arrival.

Post-mortem: The dura was slightly adherent to the pia. There was considerable hyperæmia of the vessels and numerous subpial hæmorrhages on the convexity of the brain as well as on the foremost part of the base round the chiasma, on the lower side of the frontal lobes and in the Sylvian fissure, where the tissue was diffusely infiltrated with blood. No tubercles or gelatinous exudates could be seen. At the entry to the left Sylvian fissure, just where the left Sylvian artery arises, an aneurysm the size of a pea was seen.

Microscopic examination showed a simple rupture of an aneurysm without cellular infiltration of its wall.

The middle lobe of the right lung consisted entirely of a system of bronchiectatic cavities. Both lungs and the spleen were sprinkled with miliary tubercles. The upper mediastinal glands were caseous, otherwise nothing abnormal was found.

The aneurysm must be regarded as congenital.

A more detailed pathogenetic explanation of this case is scarcely possible; it is uncertain whether the aneurysm might have been diagnosed at an earlier date. In cases of coincidence between an aneurysm and other intracranial disease the diagnosis of the aneurysm will as a rule have to be excluded beforehand. In two cases an aneurysm, which had not ruptured, was found as an accidental post-mortem finding in cases of organic encephalopathies.

The first case was an old woman, aged 64 (Case 11), who had a soft (arteriosclerotic?) aneurysm, scarcely the size of a plum, on the left ophthalmic artery just before it passed through the foramen opticum. The aneurysm extended in a dorsomedial direction, was firmly adherent to the optic nerve, which it compressed, and had caused a depression, the size of a walnut, in the trigonum olfactorium. There was also an encephalomalacia, the size of a rather big nut, in the left lenticular nucleus, in addition to a smaller one high in the left frontal lobe. The Wassermann reaction in the spinal fluid was positive and there was a strongly positive reaction in blood. The history indicated two confusional states with aphasia and right hemiplegia occurring at intervals of months.

In the other case, that of an old man, aged 75 (Case 12), with senile arteriosclerotic confusion and dementia, an aneurysm about 2 by 1½ cm. in size and filled by clots was found on the basilar artery (fig. 6). Under the left temporal lobe a psammoma, about 1 cm. in size, was found and in the cerebellum a fairly large softening.

In a third case, a man aged 49 (Case 13), with encephalopathia luetica, a spindle-shaped dilatation, the size of a forefinger, was found on the basilar artery (*vide* fig. 2).

Case 13.—A married man, aged 49, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital, April 21, 1921, and died on June 5, 1921.

The father's brother died mentally ill.

About twenty-six years ago he was treated here at the hospital for mental depression. He had lues twenty-one years ago, and was treated four times with inunctions and injections, but never with salvarsan. He had had no later symptoms.

From November 7 to 13, 1916, he was treated in the Department for Mental and Nervous Diseases of the Kommunehospital under the diagnosis dementia paralytica. At that time he had already for several years suffered from "nervousness," exhaustion and rheumatoid pains in the loins and back, and in the knees, but never real lancinating pains. His state of mind was one of depression. He complained of pain in the precordia. Objectively no positive signs of dementia paralytica were found. Heart: accentuated second sound, otherwise normal. Pulse 78, somewhat high tension. Skin reflexes weak, plantar reflexes not obtained. Knee-jerk and Achilles-tendon reflexes absent. No ataxia. Otherwise no neurological abnormalities. Lumbar puncture: cells 16 with 70 red cells, albumin 40, globulin 3, Wassermann reaction in fluid positive, in serum negative. Urine normal.

His condition had later gradually grown worse, especially during the time previous to his admission. He complained of continual low spirits, irritability, bad temper and increasing loss of memory. Of late there had been a fair amount of headache, a few attacks of vomiting and periodic dizziness. From time to time he had diplopia, and rheumatic pains in the extremities, but no lancinating pains, no girdle feeling or gastric crises. His urine sometimes passed involuntarily. His gait became increasingly unsafe, especially in darkness; he had sometimes fallen and had had difficulty in getting up again. During his stay at the Department he was rather dull; it was difficult to make him adjust himself to the rules of the hospital and to respect decorum. His spontaneous speech showed some hesitation, the test words were repeated fairly well, but there was definite impairment of perception.

He was much aged and with a dull appearance; there was slight ptosis of the eyelids, the pupils were equal and did not react to light. From time to time there was fibrillation of the muscles of the face. The abdominal reflexes were present. Extremities: Some power retained, no ataxia, the tendon reflexes were lively in the upper extremities, the knee-jerks and Achilles-tendon reflexes were not obtained, even when the patient was placed on his side. No loss of sensory functions. The senses of stereognosis, locality and position were retained; he walked with a broad base, slightly tottering; Romberg's sign positive. Slight ataxia to knee-heel and finger-finger tests. Pulse regular, tense. The blood-pressure was over 240 mm. systolic. The urine did not contain pathological elements.

April 23. Lumbar puncture: fluid clear, $3\frac{1}{2}$ cells, 5 globulin, 25 albumin, Wassermann reaction in fluid positive, in serum negative.

April 23. Babinski response definite on the right side.

April 24. Examination of the eyes: Visual acuity, L. $\frac{5}{12}$, R. $\frac{5}{12}$. The patient from time to time mentioned double vision corresponding to a slight paresis of the left external rectus muscle, but after having looked at the object for some time the pictures came together. On the whole the range of all movements seemed to be diminished. The left pupil was a little larger than the right, reacted to light and well on accommodation, but defectively on convergence. Ophthalmoscopic examination and the fields of vision were normal.

He was given antisyphilitic treatment with injections of calomel and neosalvarsan.

June 4. Suddenly yesterday evening he vomited and became weak on the left side. Since then he has been flaccid, with upward-turned eyes and snoring respiration. He vomited continually and became stuporous, more restless and incontinent. The hemiparesis remained unchanged and he died next day with a moderate increase in the temperature.

Clinical diagnosis: Encephalopathia luetica (dementia paralytica?). Hæmorrhagia cerebri.

Post-mortem: On the base of the brain, especially in the cerebello-pontine angle, a hæmatomata the size of a child's hand was found, originating from an aneurysm of almost the size of a fore-finger, on the basilar artery.

The vessels of the brain were very sclerotic (fig. 2).

The heart was somewhat enlarged, the left ventricle hypertrophied. Nothing abnormal was seen on the valves, but in the descending aorta typical plate-like thickenings in the media were found, with wrinkling of the intima, and what was undoubtedly an aneurysm. The coronary arteries were rather stiff and calcified, and in the myocardium coarse patches of fibrous tissue were found.

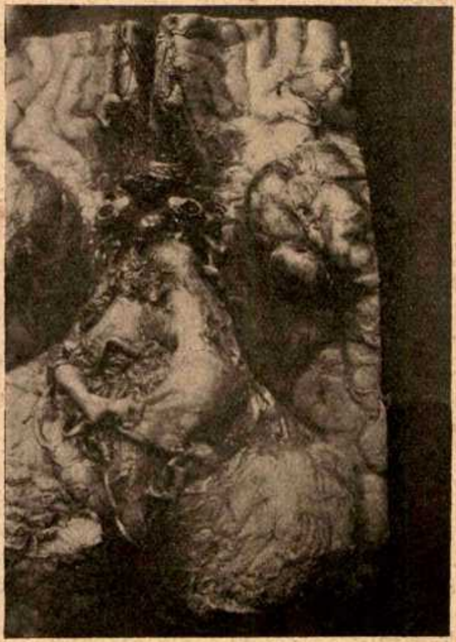

FIG. 2 (*Case* 13).—Spindle-shaped aneurysm in a man 49 years of age who suffered with endarteritis obliterans.

The kidneys were rather small, but of equal size. The capsule was easily removed, the surface rather granular; the cortex was narrow, the kidney structure obscured and the vessels distended.

The microscopic examination of different parts of the brain cortex, brain stem, cerebellum, medulla oblongata and spinal cord showed widespread arteritis obliterans of the smaller and medium-sized vessels and some perivascular infiltration with round cells, but no changes typical of dementia paralytica.

The microscopic examination of the aneurysm is described later (p. 528).

Although the symptoms of hæmorrhage in the last case were rather characteristic, it was, as in the two other cases, impossible to diagnose during life.

It will be evident from what has been stated that in hæmorrhage from an intracranial aneurysm there is no pathognomonic symptom by which an aneurysm may be diagnosed. But the course of the hæmorrhage may suggest in some cases (and more frequently than has hitherto been the case) that it originated from an aneurysm, especially when there are symptoms of impending rupture. If before the hæmorrhage there had been local or focal symptoms the diagnosis may be made with reasonable certainty.

On the other hand, when the aneurysm has not given rise to hæmorrhage it is very important to make the right diagnosis on the local symptoms from the point of view of treatment; partly because in most cases an operation carried out on the diagnosis of tumor cerebri would be fatal on account of the hæmorrhage, partly because of the possibility of a rational treatment of the aneurysm if the diagnosis is made in due time. In some cases the clinical picture is so characteristic that it is possible to make a diagnosis. In the cases of Beadles the aneurysms on the basilar artery gave symptoms before the bleeding began in 50 per cent. of the cases: those on the posterior communicating artery in 47 per cent.; those on the posterior cerebral artery in 41 per cent.; while aneurysms on the middle cerebral artery produced symptoms in 22 per cent. only. Aneurysms on the internal carotid artery in its course through the sinus cavernosus caused symptoms in 69 per cent., those in the rest of its intracranial course only in 31 per cent.

The aneurysms on the basilar artery are thus those which most frequently cause symptoms (excluding the intrasinus aneurysms on the internal carotid artery), and the most characteristic clinical picture; if the latter is not clear cut, the diagnosis is difficult. Krabbe and Backer (1922) collected cases of the latter type from the literature, and have at the same time reported one new case and sketched the clinical picture. The most characteristic symptom is the appearance of temporary slight hemiplegia alternately on the two sides, the consequence of pressure first on one, then on the other pyramidal tract (Carl Lange, 1872). In addition to pyramidal symptoms and possibly sensory disturbances, paralysis of different cranial nerves, depending on the site of the aneurysm, may be found, e.g., in the upper part of the basilar artery the oculomotor nerve suffers; aneurysms of its middle and lower parts may affect the trigeminal, abducens, facial, acoustic and even the posterior cranial nerves. These may be combined in different ways; as a hemiplegia alternans or quadriplegia; one limb may be only slightly paralysed; or there may be deafness, difficulty in speaking, swallowing, or respiration, or radiating pains of different kinds, besides the characteristic headache, which as a rule is localized to the back of the head. Comte rightly emphasizes that the patients as a rule are psychically intact up to the time of death.

Of my five cases one shows such a picture:—

Case 14.—A man, aged 66, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital: (1) January 5 to February 14, 1908, and (2) September 4, 1914, and died there September 7, 1914.

He had been healthy before, apart from a series of traumata, including some of the head, as for example falling from a height of about 40 ft. This was followed by a stay in hospital for seven weeks. There were no paralyses or other sequelæ of the accident. In May, 1907, he began to feel ill with pains in "the throat" on bodily effort. The pain started in his palate and passed through his neck down to his chest Nine days before admission he had "pneumonia" (?) with very high fever. He had difficulty in speaking during the first days and talked a lot of nonsense. From the beginning of the disease there was severe headache on the right side and severe pains in the right side of his throat, and in his right shoulder and upper arm; on the third day severe vomiting set in. He had also for a couple of weeks had pains "like a wound in the mouth," radiating up to the right orbit. On admission he was highly feverish with herpes labialis. He appeared to be in pain. The expression of the face was somewhat mask-like, the right angle of the mouth slightly drooping and the right nasolabial furrow slightly smoothed, with slight ptosis of the right eye and overaction of the frontal muscle. The right pupil was smaller than the left. The tongue and soft palate were moved naturally. The cranium was rather irregular with a great depression corresponding to the coronal suture. The tendon-reflexes of the lower extremities were absent on both sides. Babinski's sign was absent. The chest did not show anything abnormal,

January 7, 1908. Condition of pupils unchanged. Ptosis evidently diminished. The tendon-reflexes to-day were lively on the left arm and all present, but very slight on the right side, and the muscles were flaccid. He was somewhat uncertain on finger-to-finger test and finger-to-nose test with the right hand. There was slight hyperæsthesia and hyperalgesia on the right side of the forehead, the temple and especially the back of his neck, and also on his shoulder, and diffusely all over the right hand and arm. On the left upper extremity perhaps some hypalgesia and hyperæsthesia. When lying on his side the knee-jerks were very lively, the right ankle-jerk was feeble, the left fairly brisk.

The urine contained no pathological elements. Temperature normal. Examination of throat for diphtheria negative.

On the following days he complained of pains in the right side of the head, especially over the right supra and infra-orbital foramina and in front of the right ear.

January 16. Pains in the face diminished.

January 21. Right pupil is still only the size of a pin, but reacts to light. Knee-jerks now lively; tendon reflexes in both upper extremities lively. No Babinski response. Evident hyperalgesia on right foot and leg. Sense of localization and position a little uncertain on the right foot On the rest of the right half of the body a tendency towards hyperalgesia.

January 25. No special complaints. The tip of the tongue diverted a little to the right, and the right angle of the mouth drooped. Reflexes present. Hypalgesia on left upper extremity, but no other loss of sensory function.

February 14. Discharged well.

Clinical diagnosis: Influenza with pneumonia.

He had not been well since, but had had pains in both legs, every evening, with pains in the throat and in his right arm The day before readmission he became more weak, could not stand on his legs, nor had he any strength in his arms; he complained of severe headache, and was drowsy.

On examination he had an aged appearance; the right angle of the mouth drooped. His tongue moved normally He talked slowly. The pupils were equal, contracted and reacted to light. Reflexes on both upper extremities lively, no clonus. Knee-jerks not obtainable. No loss of sensory functions.

Heart and lungs: emphysema. Heart sounds faint. Only slight peripheral arteriosclerosis. Temperature 38·3° C.

Some hours later he was restless and confused and had difficulty in speaking and in swallowing, but was conscious, explaining himself by means of signs. The left pupil was bigger than the right, both reacting slightly to light. Paralysis on the left side of the face, was noted and considerable paralysis of the left leg and of the left arm, with increased tendon-reflexes and obvious Babinski response, together with reduced sensitiveness on the left side. He quickly became weaker, developed Babinski's responses on both sides and Leri's reflexes and died with increasing hyperthermia, but was conscious till the end, on September 7.

Post-mortem: On the base of the pons a considerable dilatation of a very sclerotic basilar artery was seen, which in one place formed an aneurysm twice the size of a nut, with thin, discoloured, translucent walls, filled with fine cobweb-like adhesions. Similar adhesions were found all over the base, forming a net over the fissures and the arteriosclerotic vessels The brain was not further examined.

In the aorta arteriosclerotic changes were especially pronounced in the arch and in the lowest part of the abdominal aorta. The iliac arteries were almost totally calcified. At one place in the beginning of the thoracic aorta a large whitish cushion-like thickening was found. In the ascending part just above the aortic valves small nodules, cicatrices and an arteriosclerotic patch, the size of a sixpence, were found. The heart weighed 570 grm. There was considerable hypertrophy of the wall of the left ventricle, not of the right. There was atrophy of the papillary muscles on the posterior valve of the mitral and of those in the right ventricle, and at the apex of the ventricle a parietal thrombus, the size of a rather big nut. The myocardium was abnormally firm with considerable nodular areas of fibrous tissue. The coronary arteries were arteriosclerotic.

The kidneys were atrophied with a greatly narrowed cortical zone, the capsule adherent, the surface finely granulated, the structure well marked. The urinary organs were otherwise normal. Microscopic examination of the aorta revealed pronounced thickenings of the intima and calcification on the border of the media with doubtful inflammatory changes.

The corpse was strongly built, and well nourished; weight 56½ kg.

In this case the local symptoms were characteristic, while on the other hand the symptoms of bleeding were indefinite. But the picture of the disease did at least point in the direction of an aneurysm on the basilar artery. The increase of temperature on admission was probably caused by the hæmorrhage, as in the hospital it was impossible to find anything abnormal in the chest. The adhesions, fine as a veil, all over the base of the brain are, though not common, yet clearly an expression of repeated small bleedings from the aneurysm. Whether the aneurysm in this case was syphilitic, it was not possible to decide. According to Saadhoff, syphilitic aneurysms are mostly found on the basilar artery.

In a previous case (No. 13) the aneurysm on the basilar artery did not give distinct independent symptoms, and on account of the complicating luetic encephalopathia could not be diagnosed. In the third case (No. 12) the aneurysm produced no recognizable symptoms and was unruptured. In the fourth case (No. 10), already mentioned, information was not obtainable, but the combination with miliary tuberculosis excluded, I think, the possibility of diagnosing an aneurysm. In the fifth and last case (No. 16), where, in a 40-year-old woman, a ruptured aneurysm the size of a cherry was found on the basilar artery, no information was available, as the patient was admitted in a state of coma and died soon after.

An aneurysm on the internal carotid artery, which is the most frequent site in my material, also often gives symptoms, especially when situated in the cavernous sinus (in 69 per cent., Beadles). In these cases compression of the nerves which run in the wall of the sinus is found, with paralysis of the eyes, neuralgia of the ophthalmic nerve, and perhaps also compression of the optic nerve. On rupture an arterio-venous aneurysm with pulsating exophthalmos is formed. Aneurysms in this part of the artery do not occur in my material. Aneurysms on the first intracranial part of the internal carotid artery may also cause characteristic clinical pictures, as shown by Paul Møller amongst others, but the symptoms are far from constant. The most frequent are increasing paralysis of the eye muscles and diminution of vision, perhaps optic atrophy on the same side, accompanied by headache, and later also trigeminal symptoms. Besides total internal and external ophthalmoplegia there may be paralysis of the facial nerve, and these symptoms may be combined in different ways. Such a case is the following (published before by Harald Møller):—

Case 15.—A woman, aged 53, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital, January 1, 1916, and died there January 2, 1916.

From her earliest childhood she suffered much from headache and at any rate for the last thirty-two years had attacks of violent pains in her head, which occurred once or twice in the week; they were unilateral, most violent at the back of her head and in the right side, but also in the left side. Sixteen years ago a decrease of the sight of the right eye was noted; five years later paralysis of the eye muscles and considerable loss of the vision of this eye set in, and nine years ago complete blindness of the right eye and ophthalmoplegia. A year ago spasmodic pains developed in her right eye and around it, and also a typical neuralgia in the first and second branches of the right trigeminal nerve. The pains constantly increased in spite of large doses of morphia. During the last days before admission the pain had been very violent; she became comatose on the day of admission.

On admission she was comatose. The right pupil was dilated, no paralysis of the face, the reflexes in upper extremities were increased, knee-jerks not obtained, from both feet a Babinski response could be elicited.

Post-mortem: On opening the cranium a large hæmorrhage was found, stretching on to the convexity, but it was most pronounced on the base of the brain and especially round the anterior poles of the temporal lobes. In the right middle cranial fossa, near the basi-sphenoid, a thin-walled aneurysm was found, scarcely the size of a chicken-egg, partly filled with coagulated blood. The cavernous sinus was not seen. The right optic nerve was compressed; between the aneurysm and the tip of the petrous bone were found the remains of the Gasserian ganglion. On the internal side of the base of the right temporal lobe there was an impression of the aneurysm.

In the aorta there were diffuse thickenings of the intima; the left ventricle of the heart was hypertrophied, and slight sclerotic changes were found in the coronary arteries. The kidneys showed chronic nephritis.

The aneurysm seems to have been congenital.

The history of her disease does not give any information of a previous rupture, yet the case is so characteristic, not least its protracted course, that a probable diagnosis might have been made. A series of similar cases has been reported from different quarters, amongst others by Taylor Harris and by Conway; in Conway's case there was a paroxysmal increase in the headache on effort (lifting of burdens, &c.). But there is also a series of cases in which the aneurysm has compressed the chiasma and produced a picture similar to that of a tumour of the hypophysis with bitemporal hemianopia leading to optic atrophy on both sides (in the cases of Kümmel even dystrophia adiposo-genitalis).

Case 16.—A woman, aged 40, married, was admitted to the Department for Nervous and Mental Diseases of the Kommunehospital, January 26, 1919, and died there January 27, 1919.

She was admitted in coma. She was said to have been healthy up to a year ago, when she observed that the vision of her right eye became weaker, and about the same time she got severe headaches, especially localized to the neck. The vision in her right eye diminished, and she became blind in this eye. About three months before admission the vision of the left eye also began to weaken and became very reduced. The headache increased and had been very severe and constantly present. No acromegalic symptoms. Psychically nothing extraordinary.

On the day before her admission she suddenly had an attack of unconsciousness. There were also said to have been convulsions which lasted for several hours in which she bit her tongue and passed fæces involuntarily.

She was admitted in a deeply unconscious state, and did not react when addressed The right pupil was larger than the left, and did not react at all to light; the left pupil only reacted slightly and slowly. No marks of tongue-bite.

Heart and lungs healthy. Temperature 39°C Pulse strong and regular 76.

She seemed unable to move her left arm; the triceps reflexes were absent, the ankle-jerks and knee-jerks weak. A trace of Babinski response on both sides. She died within a few hours.

Lumbar puncture and estimation of the blood-pressure not performed.

Clinical diagnosis: Coma, convulsions. (Tumor cerebri ?)

Post-mortem, January 28: When the brain was removed a considerable infiltration by blood of the pia mater at the base of the brain was found, reaching forward on the right side over the orbital roof where there were several fairly large flat clots. After removing these, a spherical aneurysm was seen, the size of a plum, on the right internal carotid artery, ending exactly at its division and lying on the optic chiasma which was very much compressed by the aneurysm. It had formed a cavity in the brain tissue (in the fossa interpeduncularis) and compressed the stalk of the hypophysis which lay behind it, together with the hindmost part of the olfactory tract, especially on the right side. The aneurysm, which lay slightly to the right of the middle line, had ruptured on its anterior and inner surface and was partly folded together, but it still contained some fresh coagula. Considerable infiltration of blood was found in the lower medial part of the right frontal lobe, which was softened (fig. 3).

Earlier and more recent tuberculous changes were found in both lungs together with an open foramen ovale in the heart.

The aneurysm was supposed to be congenital.

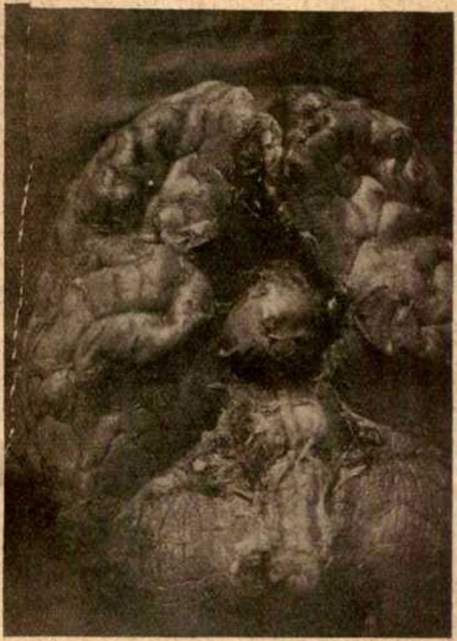

FIG. 3 (*Case* 16).—A burst aneurysm the size of a plum, on the right internal carotid artery, in a woman 40 years of age.

Before a case such as the above gives symptoms of hæmorrhage, it is almost impossible to make a differential diagnosis from a tumour of the hypophysis. To this must be added that aneurysms on the internal carotid artery not seldom cause destruction of the bones, especially destruction of the sella, which in no way differs from the destruction caused by a tumour of the hypophysis (Albl). In this case the only possibility of making the differential diagnosis occurs when the aneurysm contains so much calcium that it gives a shadow of its own on the skiagram (*vide infra*).

In Case 9 an aneurysm, the size of a hazel-nut, on the internal carotid artery had not given subjective symptoms before the rupture;

even though the optic nerve was found stretched over its front wall, there had been no complaint of defective vision. In the case of a 59-years-old woman with definite lues spinalis (tabes ?) a ruptured aneurysm, the size of a pea, was found on the internal carotid which had not given symptoms apart from the fatal hæmorrhage. One year before, ophthalmoscopic examination had, except for Argyll-Robertson's symptom, shown normal conditions. A fifth case (No. 3) had given no symptoms previously; in the sixth and last case the history and the examination are not complete (the patient died on arrival at the hospital).

Aneurysms on the ophthalmic artery are not likely to give characteristic symptoms. In the case of a 75-years-old woman with syphilis (Wassermann reaction positive in fluid) an aneurysm the size of a plum was found on this artery; two foci of softening on the same side were probably the explanation of the two attacks; that the aneurysm had mechanically caused the latter (or endarteritis obliterans ?) is possible. In cases of aneurysm here, as in the case of those on the anterior communicating and the anterior cerebral arteries, psychical symptoms are said to occur in addition to possible disturbances of vision or anosmia.

The aneurysms on the posterior communicating artery give symptoms related to the oculomotor nerve and the abducens nerve together with disturbances of the trigeminal nerve, and may in certain cases give rather characteristic clinical pictures. In neither of my two cases were symptoms present before the hæmorrhage; in one case (Case 8) after the first hæmorrhage there was a paralysis of the abducens, which might have aided the diagnosis.

Spontaneous subarachnoid hæmorrhage, accompanied by paralysis of the eye muscles, neuralgia in the trigeminal territory or optic atrophy, may on the whole be said to be indicative of the presence of an aneurysm.

Aneurysms on the middle cerebral artery seldom give local symptoms, but may cause convulsions; they are often impossible to diagnose before they burst, as in my Case 4. The convulsions are of epileptiform or Jacksonian type and are followed by transient paralysis, which later may become permanent; sometimes a permanent hemiplegia may develop due to encephalomalacia.

In two of the cases, aneurysms, the size of a pea, on the middle cerebral artery, gave no symptoms at all, neither before nor during the rupture. In a third case an aneurysm on the left side, the size of a walnut, was associated with hemiplegia of the left side and paralysis of the left oculomotor nerve. This case clearly illustrates the slight importance of the local or focal symptoms in a manifest hæmorrhage; even distant parts of the brain may give symptoms either directly owing to the hæmorrhage or indirectly owing to disturbances of the circulation. Most frequently it is even impossible to determine on which side the hæmorrhage had its origin. Bilateral convulsions were found in one of the cases mentioned, but this has also occurred with a burst aneurysm of the basilar artery. Only in one case, which in many ways is rather exceptional and therefore is reported in detail, did we find distinct focal symptoms which, as the aneurysm had not caused any hæmorrhage, led to the diagnosis of tumor cerebri.

Case 17.—An old woman, aged 66. Twenty years previously she had been infected with lues, and had fifty treatments by injections. Three years later she gave birth to stillborn twins. In May, 1907, she had attacks of unconsciousness with hemiplegia of the right side, for which she was treated at Sundby Hospital until July 14, 1907. During the stay there no signs of syphilis were observed. The paralysis disappeared fairly quickly. In 1918 she was operated on in Bispebjerg Hospital for ventrofixation of the uterus. The Wassermann reaction was not performed; during her stay no signs of syphilis were observed.

During several years she became increasingly confused and vague; she sometimes went out without being dressed, turned on the gas, cut her dress to pieces, &c. She had decreasing power of perception, but good memory for previous events; attacks of unconsciousness became increasingly frequent during the latter years. She suddenly goes red in the face, the eyes turn upwards, she cries out, becomes stiff and later flaccid. She does not remember the attacks, which are of short duration; after many of the attacks there is a temporary asymmetry of the mouth and paresis of the tongue. Later she became more irritable and unsociable and for the last one and a half years uncleanly with incontinence of urine.

When admitted to the Department for Nervous and Mental Diseases of the Kommunehospital, October 4, 1928, she was childish and slightly euphoric, smiling foolishly. There were no speech disturbances of amnestic or dysarthric nature, but she articulated rather badly: on the other hand, from time to time she mistook words. Her power of apprehension was poor, as seen in testing sensation and power of localization.

Ophthalmoscopic examination: The left pupil a little smaller than the right, both react slightly to light and well to convergence. Field of vision and ophthalmoscopy normal except for early cataract of both eyes.

Examination of ears difficult on account of inaccurate statements of the patient, but it seems to show deafness on both sides with pronounced loss to high tones, most in the left ear. This seems to suggest nerve disease and corresponds more to lues cerebri than to a tumour.

There did not seem to be anything wrong with the rest of the cranial nerves, but the tongue deviated a little towards the left, with perhaps fibrillation; the trigeminal nerves were not affected.

Upper extremities. Right: No localized muscular atrophy, but the muscles on the whole rather slack, and their strength poor. Sense of posture and stereognosis present. No ataxia. Tendon-jerks weak. Left: The general condition the same as on the right side, but the muscular strength rather difficult to judge on account of disease of the bone in the left elbow after an old fracture. Perhaps slight paralysis of the left hand, some ataxia or irregularity in the finger-to-nose test; sense of position apparently unaffected, no astereognosis; tendon reflexes weak.

Abdominal reflexes absent, abdomen large and slack. No paralysis of the bladder.

Lower extremities. Right: Muscle strength feeble, slack musculature without localized atrophy. Sense of localization and position as well as superficial and deep sensibility intact; slight irregularity in muscle movements, but no ataxia, tendon reflexes absent. Almost normal plantar reflex. Left: Similar conditions, except that the plantar reflex is sometimes of the Babinski type.

Her walk was feeble and unsteady, only a few steps were possible. It was impossible to test for Rombergism. Examination of sensibility: Brush and pin prick localized rightly everywhere. Perhaps a slight universal hypalgesia, but the statements were unreliable.

A rather obvious senile myxœdema. Spinal fluid clear, colourless, less than one cell, globulin 0 (1?), albumin 26, Wassermann and Sigma reactions in blood and spinal fluid negative, Kahn negative (by sensitized antigen positive).

X-ray: In the right temporal region small calcified shadows are seen, which are probably caused by an intracranial formation in the middle cranial fossa (see fig. 4). The left elbow shows no changes characteristic of syphilis.

During the stay here she had a series of attacks, most often in the night, beginning with a cry, followed by unconsciousness and turning of the head to the left, but no spasms or convulsions. Postparoxysmal paralysis was not seen.

As her attacks were presumed to be connected with a tumour in the right frontal lobe, and the position of the latter seemed superficial, an operation was advised.

This was performed at the Surgical Department of the Kommunehospital under local anæsthesia and slight chloroform-ether inhalation. After the dura mater was split, nothing abnormal was revealed on the surface of the brain, but the tumour was felt on palpation as a hard formation, immediately under the surface. It was enucleated easily and quickly, but was found to stretch rather far into the depth of the hemisphere. Profuse bleeding from the bed of the tumour set in during which the patient collapsed: in spite of repeated tamponades the hæmorrhage continued and the patient died a few hours later.

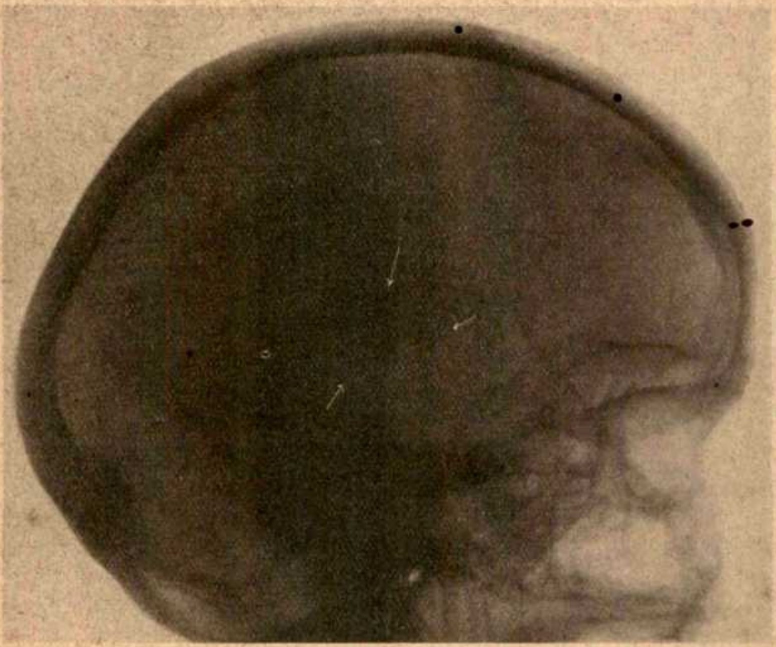

FIG. 4 (*Case* 17).—Radiogram of an intracerebral aneurysm the size of a walnut, on the right middle cerebral artery.

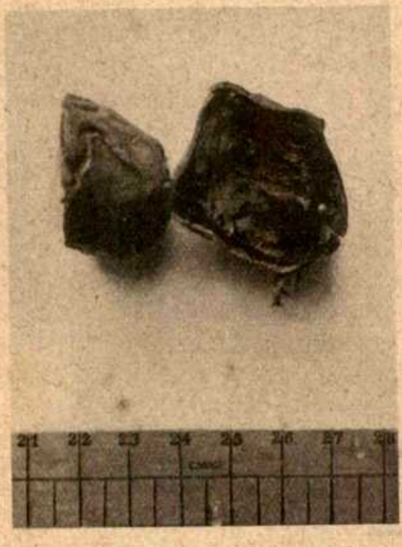

FIG. 5 (*Case* 17).—The aneurysm as removed by operation.

Post-mortem: The tumour was placed in the front part of the temporal lobe, and extended to the point of origin of the Sylvian artery. The tumour, the size of a walnut, consisted of a compact fibrous capsule and was filled with coagulated blood. In several sections of the capsule, it was found to consist of vessel wall with adventitia, a somewhat atrophied and frayed media, together with a thickened, atheromatous and arteriosclerotic intima. There was no sign of syphilis in the vessel wall (see fig. 5).

Microscopic examination of the medulla oblongata, cerebellum and different other parts of the brain show no signs of active inflammation. There were moderate hyaline changes in the vessels, and in the extracerebral vessels (medulla oblongata) moderate arteriosclerosis. The meninges, especially round the medulla oblongata, were thickened. Arteriosclerotic thickening of the aortic valves at their base, and also very marked fibrous thickening of the edge of the mitral valves, were found. The heart was otherwise normal.

There were arteriosclerotic changes stretching from the aortic valves right down to the iliac arteries. In the arch of the aorta a dilatation was seen. The wall was here very thin and at some places covered with cushion-like projections in the intima, at other places cicatricial depressions, partly longitudinal, partly asteroid.

The last case is in several ways rather exceptional, partly from its purely intracerebral position which is rare (I have not been able to find a quite corresponding case in the literature) and partly in regard to the radiograph. Characteristic shadows in radiographs of intracranial aneurysms are described by H. Albl, Algyogi, A. W. Greene, Groedel, Haas, Heuer and Dandy, Odquist, Schintz, Merrill C. Sosmann and Strøm. Sosmann, with a fairly large personal material, obtained shadows in five cases among twenty aneurysms on the internal carotid artery; thus he was able to diagnose them by radiograms in twenty-five per cent. These cases originate from Cushing's tumour material and show how frequently this form of aneurysm causes symptoms of tumour. The remaining instances are merely case reports, and only in the case of Greene was the diagnosis made during life. These cases taken together give a very characteristic picture: a roundish tumour-like formation, which in itself does not give a shadow, but is surrounded by thin, curved, sharply limited outlines, which take a curved or circular course with their concavity central. Sometimes they overlap or lie outside one another, corresponding to different projections of the surface of the aneurysm, as this is seldom perfectly circular, or as a result of the calcium being embedded in layers. Further, there may be other smaller, irregular, indefinite shadows, spread over the formation, their intensity and extension depending on the calcium content of the aneurysm. According to Albl, an almost closed circle of shadow is characteristic of aneurysm, but the shadows may be curved or made up of several of different curvature. It is their tendency towards a concentric or circular arrangement which is decisive, as a very arteriosclerotic vessel may give an isolated curved shadow (Albl). It is especially the bigger aneurysms which give characteristic radiograms. Sosmann has in one case found a similar picture in an arteriosclerotic dermoid cyst, and possibly an echinococcal cyst might cause a similar picture (*vide* Claessen's radiographs of echinococcus tumours).

In Nos. 9, 13 and 16 of my cases, the brains and aneurysms were radiographed after the autopsy, but in none of these cases were shadows of calcium found. In No. 9 the sella turcica was seen to be normal also. In the case of bleeding from an aneurysm it will unfortunately often be difficult in practice to get an X-ray examination made before death. In the case of local symptoms without signs of hæmorrhage, a positive X-ray picture ought to lead to the right diagnosis.

While the clinical symptoms of intracranial aneurysms vary and often are either not characteristic or are totally absent, they are in not a few cases so characteristic that diagnosis is possible, provided one remembers how relatively frequent aneurysms of the cerebral vessels are. In many cases X-ray examination of the cranium may give valuable support for the diagnosis which is often dependent otherwise on a study of the course and development of the case. Murmurs as specific symptoms of aneurysms will be discussed in detail later.

Ætiology.—In regard to the ætiology of the aneurysm, opinions differ, and are often quite contradictory. In the cases reported here the cause of the aneurysms has been uncertain. Even if an aneurysm first gives symptoms in advanced age, it is difficult to be sure whether it is congenital, or embolic-mycotic (Eppinger), when the underlying disease may no longer be determined, and especially when no microscopic examination of the aneurysm itself is made. Likewise it will be difficult to settle whether an aneurysm is caused by arteriosclerosis, or whether there is merely an arteriosclerotic degeneration of the wall of the existing aneurysm, associated with arteriosclerosis in the other vessels. In some cases, however, the ætiology is obvious.

That aneurysms may occur as a congenital deformity, Busse showed to be probable in 1920 when, out of 400 autopsies, in no less than thirty-nine he could demonstrate by careful examination aneurysmal formations on the anterior communicating artery (i.e., in about 10 per cent.); in 43 per cent. of all the cases he found different anomalies here:

simple duplication of the vessels, plexus formations, deficiency in the junction with local hypoplasia of the artery wall and such like. De Vriese had previously made similar observations which later were confirmed by Schmorl and Aschoff (*cited* by Borchardt). On the whole developmental anomalies and variations in the course of the vessels occur frequently in the circle of Willis (Winde, Wyrubow, Parnisetti). Different authors have also found aneurysms in children.

In my Case No. 10, where, in an 11-year-old girl, an aneurysm the size of a pea was found on the basilar artery, and microscopic examination showed the vessel wall to be normal and without cellular infiltration, there can scarcely be any doubt that the aneurysm was congenital. The same histological picture was found in Case 16, that of a woman aged 40 with an aneurysm, the size of a plum, on the internal carotid artery. Here the probability of a congenital origin of the aneurysm was further increased by the existence of an open foramen ovale. In young persons this ætiology is as a rule the most likely, e.g., in Case 1 (a woman, aged 23) and Case 2 (a man, aged 28). But possibly the aneurysm was congenital in other cases too, e.g., Case 15, that of a woman, aged 53, who had had symptoms for thirty-two years and possibly even from childhood.

Lebert showed in 1866 the frequent coincidence between heart-disease and intracranial aneurysms, and Church reported in 1870 the first case of an aneurysm of embolic origin; this through the work of Ponfick (1873) was fixed as a frequent form of intracranial aneurysm. Later work by Eppinger (1887), Wichern (1911), Loewenhardt (1923), Greene (1926), has confirmed this. It is no rare form; of the forty-four cases of Fearnsides, fifteen were caused by infective emboli.

In my material there is no certain case with this ætiology, but perhaps Case 8 belongs here. There is a possibility that embolic aneurysms quickly give symptoms and burst (Esser); therefore they are likely to be observed most frequently in general medical services. If they have existed for a long time, their origin may only be proved by microscopic examination. Possibly some of my apparently arteriosclerotic aneurysms, or of the cases where it was impossible to determine the ætiology more precisely, had this origin.

Traumata are reported as a cause of intracranial aneurysms, but only a few cases with such a genesis have been published (Hedinger, Menschel, Stilling); these cases are not wholly convincing. Other reported cases are examples of false aneurysms. Further, it is difficult to exclude the possibility that a pre-existing aneurysm became larger, or produced its first symptoms, after an accident. Traumata are at any rate a very rare cause of intracranial aneurysms (Orth); and I do not suggest it for any of my cases. Esser also assumes that traumatic aneurysms do not occur. No instance is referred to in Stern's article in "Traumatische Entstehung innerer Krankheiten," 2. Aufl., v. J. Schmid.

All aneurysms were originally supposed to be syphilitic (especially by the school of Heller and French authors), but now opinion is very divided. Syphilis was considered to be the ætiological factor in the majority of cases of intracranial aneurysms by Bartholow (1872), Bradford (1903), Lewandowsky (1912); among modern authors by Krabbe and Backer (1922), Comte (1925); but Eppinger (1887), von Hofmann (1894), Fearnsides (1916), Turnbull (1918), Symonds (1923), Borchardt (1925), E. John (1925), Conway (1926), Parker (1926), Zador (1927), Pollach (1928), Esser (1928), Sands (1929) consider it a rare cause, or wholly deny the existence of syphilitic intracranial aneurysms. There is however no doubt that these may occur. In the case of Krabbe and Backer the syphilitic origin was ascertained by histological examination; but, on the other hand, there do not seem to be any cases of intracranial aneurysms in the literature in which spirochætes have been found histologically.

Turnbull especially has proved the rarity of syphilitic aneurysms; there were none in his and Fearnsides' material of forty-four cases. He refers to the fact that syphilis only attacks the small arteries, producing a proliferative obliterating endarteritis, which hardly ever causes weakening of the vessel wall and dilatation, except secondarily in the larger arteries through affection of the vasa vasorum. Saadhoff considers that syphilitic aneurysms are mostly found on the basilar artery.

The importance of arteriosclerosis in the causation of intracranial aneurysms is also disputed. It was assumed as a causative factor by Eppinger (1887) ?, Burns, Fearnsides (1916), Turnbull (1918), and Kerpola (1919); while others (e.g., Hofmann and Comte) contradict this view. On the other hand, A. Jakob has recently maintained that arteriosclerosis gives rise to the formation of aneurysms and afforded histological demonstration of this. In reality arteriosclerosis is surely a frequent cause of aneurysms, as especially shown by Kerpola.

The attempt to distinguish between syphilitic and arteriosclerotic disease of the cerebrospinal blood-vessels by the pathologico-anatomical picture alone has led different observers to hold contradictory views. Without further discussion of this disputed question I shall merely state that A. Jakob in his new book maintains that amongst the changes of the vessels of the brain which are classed as arteriosclerotic in the usual sense, lesions of syphilitic origin occur and he places syphilitic arteriosclerosis as a special form of this (A. Jakob: "Anatomie und Histologie des Grosshirns," Bd. 1, Leipzig, 1927, p. 353).

Among my cases there are four in which syphilis had been proved, or the lesions revealed at autopsy suggested syphilis. Three had lues of the nervous system, while the fourth during the course of her lues in early life had a hemiplegia which had passed off without leaving symptoms.

The most evident case is No. 13 in which there was encephalopathia luica (endarteritis obliterans), syphilitic aortitis with ectasia aortæ and arteriosclerotic changes in the coronary arteries, associated with a spindle-shaped aneurysm on the basilar artery (see fig. 1). The microscopic examination of the aneurysm showed a hyaline arteriosclerotic thickening of the intima which continued into the distended part of the vessel. The elastic tissue in the media could only be faintly seen. Inflammatory processes were absent both in the media and the adventitia, and there were no changes in the small vessels of the adventitia. But on section of the internal carotid artery, intimal thickenings due to perivascular infiltrations of round cells were found, and there was some thickening of the small vessels in the adventitia.

Without entering into the relationship between syphilis and arteriosclerosis (especially in the central nervous system) it is quite justifiable to maintain that the histological appearances in the aneurysm by no means prove its syphilitic origin, but are rather in favour of arteriosclerosis. A similar picture of typical arteriosclerotic changes was seen in the aneurysm in Case 17. In the wall of the vessel no signs of syphilis were found, but the autopsy showed a combination of arteriosclerotic and syphilitic changes in the aorta, which was the seat of an ectasia. The hemiplegia which occurred in the forty-fifth year had probably been on a luetic basis; at any rate the lesion was in the opposite hemisphere to the aneurysm.

In the third case, that of a woman, aged 59, with lues spinalis (tabes?), a ruptured aneurysm the size of a pea was found on the internal carotid artery, together with universal arteriosclerosis, but no definite signs of syphilis, certainly none in the aorta. The character of the aneurysm cannot be determined now.

In a fourth case, in a 64-year-old woman (Case 11), who had died from an encephalomalacia, an unburst, thin-walled aneurysm, almost the size of a plum, on the ophthalmic artery was discovered accidentally by autopsy. Universal arteriosclerosis was found, especially in the aorta, but no sign of syphilis. Clinically she presented the picture of two cerebral softenings occurring at an interval of a couple of months. Wassermann reaction in the blood positive (0.0.0.0.100), in the spinal fluid positive (0.0.20.100). The nature of the aneurysm cannot be determined.

In a fifth previously reported case (No. 14), in a 66-year-old man, there was a considerable ectasia of the very arteriosclerotic basilar artery, together with considerable arteriosclerosis of the aorta, which at one place in the thoracic portion resembled a syphilitic aortitis. On microscopic examination of this part pronounced thickening of the intima was found and arteriosclerosis along the edge of the media in which there were doubtful inflammatory changes. Clinically there was no information about syphilis, and unfortunately neither lumbar puncture nor a Wassermann reaction was performed.

In these four cases of intracranial aneurysms in patients with cerebrospinal lues, there was in none definite proof that the aneurysm was syphilitic. Whether the syphilis might have had any influence on the development of the arteriosclerosis, as maintained by Bradford, cannot be discussed here.

In my material there is a series of aneurysms with arteriosclerotic changes, but whether the aneurysm or the arteriolsclerosis is the primary is not easy to determine. An already existing aneurysm may, like other vessels, undergo atheromatous degeneration, but there seems to be no reason why the aneurysm should be especially exposed to this (e.g., on account of abnormal circulation), the causation of arteriosclerosis is usually assumed to be an autotoxic action on the vessel wall (cholesterinæmia). Thoma, however, ascribes a certain importance to the conditions of the circulation (see later). On the other hand arteriosclerosis is so capricious in its localization and extension that a local, limited arteriosclerosis must be considered as the cause of the formation of an aneurysm, as in the following case.

Case 18.—Woman, aged 64. Died December 8, 1917.

The clinical history was of no interest (simple rupture of the aneurysm with paralysis of the oculomotor nerve).

Autopsy revealed no marked sclerosis of the vessels on the base of the brain. On the lower side of the left temporal lobe a ragged tumour the size of a walnut, of very compact consistency, was found. On incision it was seen to consist of old coagula in layers, surrounded by a thin shell, which continued in a central direction into the left Sylvian fissure. The Sylvian artery, 4 cm. from its origin from the internal carotid artery, suddenly developed arteriosclerotic changes, and became enlarged to an aneurysm the size of a walnut. In the rest of the brain there was a smoothing of the gyri especially in the left hemisphere, but no focal changes. It is strange, in this case, to find isolated arteriosclerotic changes localized symmetrically and exclusively to the two Sylvian arteries, and going on to the formation of an aneurysm only on the left side.

In others of my cases the wall of the aneurysm has shown obviously arteriosclerotic changes, while the rest of the cerebral vessels did not reveal any sign of arteriosclerosis on microscopic examination. Thus in Case 9 there were arteriosclerotic changes, thickenings of the intima, calcification and disintegration of the media, but no trace of inflammatory lesions. There were also slight arteriosclerotic changes in the aorta, but not in the rest of the vessels.

Busse also considers that arteriosclerosis plays a certain part in the formation of aneurysms on the anterior communicating artery and admits that some aneurysms only appear after the age of 40. Turnbull, on the other hand, assumes a congenital weakening of the media as the cause of arteriosclerotic aneurysms, which he considers are common, and more frequent on the intracranial arteries than elsewhere. Even if congenital abnormalities or weakness form loci minoris resistentiæ, the importance of atheroma is indisputable.

Thoma held that primary increase of the lumen of the vessel played a definite part in causing arteriosclerosis, and considered the proliferation and thickening of the intima as an arrangement for preserving the size of the lumen (an illustration of this has been reproduced by Osler). But these views do not seem to have gained general acceptance.

In cases of diffuse universal arteriosclerotic changes in the vessels of the brain, the arteriosclerosis is probably the sole cause of the aneurysm. Thus in Case 22, besides a ruptured aneurysm the size of a pea on the right Sylvian artery, there was considerable arteriosclerosis of limited portions of the vessels. In many of the cases the cerebral arteriosclerosis was diffuse, but so pronounced that it was a plausible explanation of the aneurysm.

A rather characteristic histological picture was present in Case 12 where, in a 75-year-old man with a senile, arteriosclerotic dementia and considerable universal arteriosclerosis, an unburst aneurysm was found on the basilar artery, about 2 by 1½ cm. in size. Microscopic examination

Lateral and medial to the right optic disc smaller and larger hæmorrhages were seen close to it.

There was pronounced rigidity of all four extremities. He was inclined to keep the arms rotated inwards; the deep reflexes were equal and lively with a tendency to clonus; a Babinski response was obtained on both sides; there was no stiffness of the neck; the abdominal reflexes were feeble or absent. Other examinations showed nothing special.

He died rather suddenly two hours later.

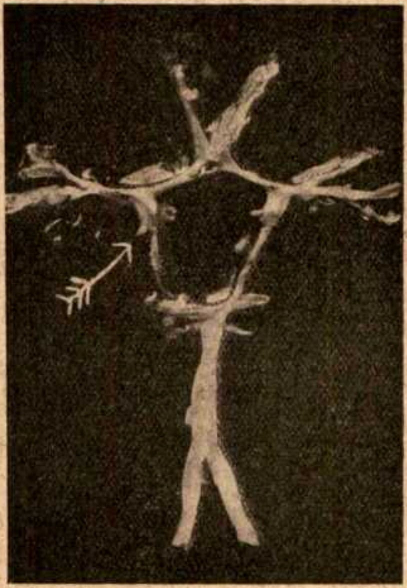

FIG. 8 (*Case* 25).—A ruptured aneurysm the size of a millet seed on the right internal carotid artery.

The autopsy fifty-six hours later at the Institute of Medical Jurisprudence showed his tongue had been bitten. A considerable subdural hæmorrhage was found, especially on the right side, with large coagula below and outward. There was also a considerable hæmorrhage in the soft membranes, most pronounced round the pons and chiasma, on the lower side of the cerebellum and at the beginning of the medulla oblongata. It was fairly symmetrical; there was less laterally and none on the convex surface of the brain. At the apex of the right temporal lobe and on its basal surface an irregular opening was found, admitting a little finger: from this one came into a superficially placed cavity, about the size of a hazel-nut and filled with blood. The walls of this cavity consisted of fairly fresh brain-tissue with diffuse punctate or streaky infiltration by blood.

After the coagula had been carefully removed, an aneurysm the size of a arachnoid hæmorrhage, surely ought to be carried out with the utmost caution and reserve. Sudden death has followed it, and in my Case 9 the operation seems to have an unfavourable influence on the hæmorrhage.

It is to be hoped that in future a greater knowledge of the clinical features of intracranial aneurysms and their characteristic X-ray appearances will enable the diagnosis to be made more frequently, and that the way will thus be opened for therapeutic procedures.

I am much indebted to my chief, Professor Wimmer, for his permission to publish the material from the Department, to prosector Dr. L. Melchior for his permission to use the pathologico-anatomical material, and to the chief of the X-ray clinic, Dr. G. Biering, for his permission to publish the X-ray photos.

ADDENDUM.

After this work was completed a new case of ruptured intracranial aneurysm (diagnosed *intra vitam*) occurred in the Department for Mental and Nervous Diseases at the Kommunehospital.

This case is of great interest as a supplement to the preceding, the aneurysm being so small that only a very carefully performed autopsy revealed it.

A married man, aged 38, was admitted to the Department for Mental and Nervous Diseases in the Kommunehospital on February 11, 1930, and died there two hours later.

He had syphilis twelve years ago and was at that time treated in the Department for Skin and Venereal Diseases at the Kommunehospital. For many years there was incessant abuse of alcohol, which suddenly ceased two months ago when he was out of work. Otherwise he had been healthy.

During the last month he had complained of a headache. About two hours before admission he came home complaining of a severe headache. He went to bed, but a moment later got up again complaining of a rather strange taste in his mouth, and shortly after he fell unconscious to the floor. Soon after this he had convulsions.

When admitted he was still in convulsions, but they soon ceased. He was unconscious, pale and slightly cyanotic. The rectal temperature was 37·1° C., respiration bout 20, rattling, slightly snoring; pulse 76, regular, strong; blood-pressure 150/90. The pupils on both sides were rather dilated and did not react to light. The right eye was slightly divergent outwards and upwards. Ophthalmoscopic examination showed the edges of the optic discs normal, perhaps a little blurred; the vessels curved, twisted and distended.

into an aneurysm, which compresses the optic nerve. Apart from the murmur the patient is now subjectively well.

It is noteworthy that the blowing noise could only be heard on direct auscultation, and not with a stethoscope: this has not previously been reported in the literature. This may perhaps explain why murmurs are so seldom noted in cases of aneurysms on the cerebral vessels, but it is probable that so unpleasant a symptom would have been complained of by the patient and, if really a frequent symptom, would not have escaped mention. In future it will be advisable to auscultate the cranium directly, in any case where the possibility of a brain aneurysm exists. Bing tries to explain the audible murmur by the fact that the aneurysms are nearly always placed on the base, and therefore the sound is conducted directly by bone especially through the great wing of sphenoid; but evidently this is not the explanation, at any rate not in the present case.

Treatment.—The therapy of intracranial aneurysms has until now only given very poor results, which is mainly due to the difficulties of diagnosis. In some cases operative intervention has been tried, usually on the supposition that a tumour was present. In one case Cushing vainly tried to remove an aneurysm; later he ligatured the internal carotid artery instead, but this treatment caused hemiplegia, which partly disappeared later. Ranjard is said in two cases to have gained good results by ligature of the intracranial part of the internal carotid artery, and Coe and Lefort have also successfully used operative treatment. Forster (after Borchardt) has in one case been successful by a decompressive craniotomy. In view of the serious prognosis of aneurysms, at least when signs of hæmorrhage or impending rupture are present, operation is justified; when hæmorrhage has occurred the result will possibly be doubtful. The best method is ligation of the supplying vessel, especially the internal carotid artery after temporary compression of the common carotid artery in the neck, to avoid a hemiplegia. In cases of pulsating exophthalmos where, however, circumstances are not quite the same, this treatment has not always given satisfactory results. Extirpation of an intracranial aneurysm with good results has not been reported in the available literature, even though in several cases it might have been technically possible (Borchardt).

On account of the diagnostic difficulties therapy must, as a rule, be conservative, which most frequently means preventive. Gelatine injections may possibly have some effect in bleeding aneurysms. Lumbar puncture, although of therapeutic importance in other forms of sub-

infection called influenza; a couple of weeks later he began to get extremely violent pains which radiated from his left ear up into the scalp. Some weeks later similar pains occurred in the right side of the head. The patient was extremely sensitive to changes of temperature and had great tenderness of the scalp, though perhaps not in the neck. Both temporal arteries were firm and thickened; later during the disease first the left temporal artery and then the right thrombosed, and became pulseless; now nine months after the onset of the disease, the pulse is still absent from the right one and only doubtful in the left. The patient was slightly febrile with temperatures between 38° and 38·5° C. for two to three months; he was in great pain and had much aspirin, atophan, allonal, cibalgin, quinine, &c., but it was not necessary to use morphia. Among the numerous antineuralgic remedies used only aspirin seems to have had any definite effect; he had up to 8 grm. in twenty-four hours. In addition he was treated with courses of sudorifics. The patient became much weaker during this period; he suffered very much from perspiration, ate only very little, and lost 6 kg. in weight. After two to three months the pains grew less and he got out of bed.

As the diagnosis was difficult, the patient was examined by Dr. K. H. Krabbe for neurological signs, by Dr. Frants Norsk for evidence of disease of the ear or throat, and by Dr. Collin who radiographed his cranium, but nothing further was discovered.

During the disease an anæmia developed which was treated by injections of arsenic without effect; only when in June and July he went into the country, and at the same time began to eat powdered liver, did a remission take place.

Date	Hb.	Erythrocytes, million	Erythrocytes, vol.	Index, colour	Index, vol.
24/4	76 per cent.	3·9	29·5	0·97	0·87
1/5	66 ,,	3·9	34	0·83	1·01
3/6	65 ,,				
30/8	83 ,,				

During the summer the pains disappeared completely, and he was completely all right, and even partook in many parties, considering his age.

One day in August he suddenly had a feeling as if he had a one-cylinder motor in his head and at the same time, or almost at the same time, a cloud over the right eye. There was no pain and the condition of the patient was otherwise unchanged.

Ophthalmic examination by Dr. Fabricius-Jensen showed his visual acuity to be $\frac{5}{6}$. The right pupil was a little bigger than the left, but reacted normally. Ophthalmoscopy showed fine senile degeneration in the retina, but nothing pathological. Tension normal. In the right field of vision there was a complete paracentral scotoma for white and colours, and in continuity with this a relative scotoma with indefinite edges. The outer boundary for white and red was normal. The blind spots were of normal size (see fig. 7). The left field of vision was normal.

syphilitic origin are relatively rare. Corresponding with this, C. H. Sattler, among 352 cases of exophthalmos, only found one case of syphilitic origin. Thus the finding of tertiary syphilis has no diagnostic value, as maintained by Krabbe and Backer.

Noises in the head, which these authors mention as a diagnostic point, are unfortunately rare. They are but rarely observed, and are not in any way pathognomonic, as they are also found in tumours compressing larger vessels (Zador), in anæmic women (Oppenheim), in Graves' disease (Gowers) and in arteriosclerosis of the vessels of the brain (Wallenberg), although in this case they may be due to a small aneurysm. This phenomenon is a subjective feeling of ringing or pulsation, "like a machine working inside the head;" the sound is said to be also distinctly heard on auscultation of the cranium with a stethoscope. In cases of arterio-venous aneurysm between the internal carotid artery and the sinus cavernosus noises in the head are common (Ehlers). Bing reported a case of presumed intracranial aneurysm (not verified by autopsy); a 17-year-old woman who suffered from disease of the heart, presumably caused by a patent ductus Botalli, heard a pulsating jangle especially in the right ear; the sound could not only be auscultated over the whole cranium, but was also to be heard at a distance of 8 cm. Another characteristic symptom was mistiness of vision increasing to short attacks of blindness on effort, for example, when she sat up in bed.

Dr. E. Warburg has demonstrated to me a rather similar case, and has been so kind as to put it at my disposal, for which I wish here to offer him my best thanks. In this case I feel quite justified in making the diagnosis of intracranial aneurysm.

Case 24.—69-year-old landed proprietor.

The patient is a vigorous man, who looks much younger than his age; the greater part of his life he has lived in the country under good conditions; he is a moderate smoker and has never taken wine to excess. Has never had syphilis. Wassermann reaction negative. From his youth onwards he has had very severe "rheumatic" myalgia for which he has been treated several times with physiotherapy. In 1923 he had a long febrile attack with violent myalgia, for which he was treated at a health resort for three months with sulphur oil injections. His condition became considerably better, his temperature returned to normal, and after a stay in Gastein he felt almost cured.

In August, 1928, the patient had a typical attack of gout in both hands, which vanished in a few weeks under treatment with atophan. He then felt completely well till early in 1929 when he and his wife got a slight febrile of the aneurysm showed that its wall consisted in large part only of adventitia in other places also of intima together with broken plaques of media. The whole lumen was completely filled up with thrombotic masses. In the best preserved part of the vessel wall arteriosclerosis was seen in the intima and slight infiltration of round cells in the adventitia. The latter is probably associated with the absorption of the thrombotic masses (Paul Møller).

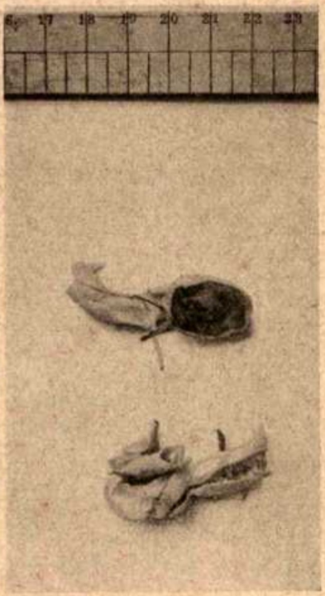

FIG. 6 (*Case* 12).—An arteriosclerotic aneurysm of the basilar artery which was found at autopsy in a man who died with senile dementia and softening of the cerebellum. The aneurysm measured 2 × 1½ cm. and was filled with a stratified clot.

Thus of my twenty-three cases four are found in persons with syphilis in the central nervous system (*vide supra*). Of the remaining nineteen, eleven are classed as arteriosclerotic, since they showed undoubted arteriosclerotic changes either microscopically or macroscopically, and no evidence of any other origin was found. Even if in one or two of these there may have been some other cause, the number is still remarkably large. Fearnsides also found a remarkable number of arteriosclerotic aneurysms. In addition five (as already mentioned) are congenital, and one perhaps infectious (embolic-mycotic, Eppinger), while the cause of the two last cases is uncertain. The probability is that arteriosclerotic aneurysms are frequent and aneurysms of undoubtedly

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NOTICES OF RECENT PUBLICATIONS.

Die diagnostische Bedeutung des Rossolimoschen Reflexes bei Erkrankungen des Zentralnervensystems., von S. GOLDFLAM. S. 274. Berlin: S. Karger. 1930. Price 24 M.

A consequence of the selective incidence of hypertonus in the extensors and plantar flexors of the lower limb in lesions of the pyramidal system is that percussion of any part of the foot elicits a "stretch reflex" of the plantar flexors of the toes, with a down-going movement of the toes. The phenomenon has the same significance as a heightening of the tendon-jerks obtained elsewhere in the limb.

It is clear that one can chose any one of a great number of spots on the foot from which to elicit this response, but that in each case the reaction is the same one, and that there is no justification in naming a series of different "reflexes" simply because a single response is elicited from different parts of the receptive field.

Unfortunately, this is what has occurred and a very simple matter has been rendered unnecessarily complicated and mysterious as a consequence. Rossolimo found that the response could be elicited by percussion on the sole of the foot over the balls of the different toes, and thus neurological literature had been endowed with Rossolimo's reflex. Bechterew, percussing the point of the heel, discovered Bechterew's heel reflex. Two observers, choosing the site of extensor brevis digitorum on the dorsum of the foot gave us the Mendel-Bechterew reflex, while Shukowski preferred the middle of the sole and Shukowski's reflex is the result.

It is to be hoped that with the greater knowledge of the physiology of the tendon reflex that is now available, this undesirable and unscientific practice of attaching the names of individuals to these reflex phenomena, and of regarding the latter simply as mysterious diagnostic symbols, will cease, and that a more rational outlook will be adopted.

Goldflam is not, however, concerned with the physiology of the Rossolimo phenomenon, but simply with its value as a diagnostic trick for the early recognition of pyramidal affections. He records in the present monograph its occurrence throughout the wide range of known affections of the nervous system and compares its value from this point of view with that of the Babinski phenomenon. He concludes that it is sometimes present before the latter makes its appearance.

The book is very diffusely written, frequently deviates into topics quite unrelated to its title, and includes numerous case records that are too incomplete to be of any value.

Syphilis héréditaire du Système nerveux. Par L. BABONNEIX. Pp. 429. Paris: Masson et Cie. 1930. Price 60 francs.

The author has collected and arranged within the present volume his numerous published contributions upon the subject of hereditary neurosyphilis. Designedly, he has produced not a formal treatise upon the subject, but a documented exposition of his view that hereditary syphilis plays a fundamentally important part in the causation of a great number of the neurological disorders of infancy and childhood.

His inclusion of Sydenham's chorea within these disorders will indicate how widely he has cast his net, and also upon what scanty evidence he is at times prepared to find confirmation of his views. In fact, throughout the book, which contains very numerous case summaries, the reader will be struck by the tenuous character of the evidence upon which the author is ready to invoke hereditary syphilis.

It is, perhaps, as an exhaustively elaborated piece of special pleading, in favour of the conclusion that hereditary syphilis plays an almost universal rôle in the causation of chronic neuro-muscular disorders in early life, that the book will have its chief interest for the experienced neurologist.

Techniques histologiques de Neuropathologie. Par IVAN BERTRAND. Pp. 376. Paris: Masson et Cie. 1930. Price 50 francs.

This volume on neurohistological technique does not purport to be a complete record of all the methods which have been used for the study of the nervous system. But it is none the less remarkably complete and up to date. The methods are clearly and fully set out, and reference back to other methods is as far as possible avoided. The last sections, dealing with the staining of degeneration products, glycogen, calcium, iron and blood derivatives, are particularly useful. The section on Marchi's method also gives some valuable advice on the recognition of artefacts, but less help than might have been hoped for in avoiding them. One is tempted to criticize the method recommended for cutting off the skull-cap by means of chisel and hammer only, without using the saw. It is also remarkable that a solution of formalin in water rather than in saline is still used in the laboratory of the Salpêtrière.

It is disappointing to note the omission of many of the useful tips which were to be found in the little book on the same subject by Roussy and Lhermitte. Such were the use of acid balsam for preserving the colour of Van Gieson's counterstain and of cedar-wood oil as a mountant for Nissl sections. The author's technique for the use of infra-red light to bring out certain of the finer points in the structure of nerve-cells appear to be too complicated for any but special research work, but it is valuable to have it incorporated in this book. Taken as a whole the book includes so much that is new or scattered in foreign journals that it is a valuable addition to the library of any research worker in neuropathology.

Études neurologiques. Troisième Série. Par G. GUILLAIN. Pp. 543. Paris: Masson et Cie. 1929. Price 70 francs.

The two preceding volumes in this series have already been noticed in this Journal, and like them the present volume contains a number of clinico-pathological studies, cast in the form of lectures and articles, and taken at random from the whole field of neurology. By design new and original work is excluded from the series. The majority of the thirty-three studies have already been published in medical journals.

They are of interest in that they exemplify the manner of approach adopted at the Salpêtrière in the investigation, and demonstration to students, of clinical material.

Die Röntgenbehandlung der Nervenkrankheiten. Von O. MARBURG und M. SGALITZER. S. 213. Berlin: Urban und Schwarzenberg. 1930. Price 15 M.

The authors provide an exhaustive review of the literature of the treatment of the various affections of the nervous system by Röntgen rays. The volume is divided into a general and a special section. In the former, full technical details of the treatment of nervous diseases is given, while in the latter under clinical headings are grouped a review of the literature, case records and complete information as to dosage and modes of application. An admirable and critical summary concludes each such section. There is a comprehensive bibliography.

The book may be recommended as of value to the neurologist and to the radiotherapist.

Handbuch der Geisteskrankheiten. Herausgegeben von OSWALD BUMKE. Sechster Band, Spezieller Teil II. Berlin: Springer. 1928. S. 376. Price Rm. 37.70.

This volume of Bumke's Handbuch contains two authoritative monographs. In the first Professor Lange presents the sum of our present knowledge concerning the affective psychoses and related conditions. As the pupil and colleague of Kraepelin, he naturally accepts the general Kraepelinian nosology, but with appropriate and adequate adaptation to modern notions. On many points he has put forward less rigid and dogmatic views than in his own earlier writings; this is evident, for example, if one contrasts his 1926 paper on melancholia with many passages in the present work. There can be no doubt that this will take the place of Stransky's earlier monograph; it is complete, and thorough to a fault.

The second part of the volume, devoted to paranoia and related conditions, is by Professor Kehrer. It is written from a definite personal standpoint, but anyone who has wandered through the wilderness of paranoia literature will welcome this. It is predominantly clinical, with illustrative case histories; the relevant literature is appraised in its degree. It is impossible to consider here his delimitation of the paranoia concept to cover only disorders in which the mental picture is more or less restricted at all times to logically grounded delusions entirely comprehensible as to motive and content, it is at any rate acceptable and precise, like the rest of the monograph. There is no glossing over difficulties or offering of fanciful solutions.

Die Prognostik der Endogenen Psychosen. Von FRIEDRICH MAUZ. Leipzig: Georg Thieme. 1930. S. 121. Price Rm. 7.50.

In these prognostic studies the influence of Kretschmer is predominant. There is a brief historical introduction in which the author traces the development since Kraepelin of psychiatric thought about the endogenous psychoses finishing with Kretschmer's formulation of the problem as to how far heterogenous mixtures of constitution influence the form and course of the psychosis. His own investigations were carried out between 1923 and 1928, and represent in the main an attempt to answer this question. The bulk of his cases were schizophrenic—1,050 out of a total 1,470. The observations were of necessity not all made by the author, which is a disadvantage. His diagnostic criteria are those of conservative German writers, in his views of schizophrenia he follows the Berze-Gruhle presentation. On the whole he finds more prognostic significance in the habitus and diathetic proportion of the "affect-psychoses" than with schizophrenia, though in all the endogenous psychoses he considers that pyknic build and "fresh" cyclothymic premorbid temperament suggest a favourable outcome. The necessity for taking all the data into consideration is made clear, and penny-in-the-slot prognosis receives short shrift. The work is clearly written and touches on many interesting points, especially of classification.

Social Control of the Mentally Deficient. By S. P. DAVIES. London: Constable. 1930. Pp. 389. Price 13s.

The importance of the social aspects of mental deficiency needs no stressing nowadays; the present work is a valuable contribution in this field. After a review of the measures adopted for the care and training of the feeble-minded since the time of Itard, the eugenic problem is taken up and the case for sterilization examined with temperate caution. The "social indictment" against the defective is shown to be overdrawn, and the more or less controllable factors which lead to antisocial behaviour are demonstrated. Where through special institutions, colonies and community supervision, socializing influences of a beneficent kind are operative, a large proportion of the feeble-minded cease to be social liabilities; the author brings evidence to show that they become social assets, but to this many would demur. The negation of good doctrines, however, is found in a quotation, "rather vivid and perhaps extreme," from Pitkin, in which the advantage and even desirability of a population of morons is supported, inasmuch as they are better fitted to our industrial civilization, more contented and healthy, than people of high intelligence.

The author points out the inadequacy of intelligence testing, used alone, and gives a convincing exposition of the social criteria of deficiency. Many widespread errors are disposed of. The book fully covers the ground which its title suggests; it is written with obvious enthusiasm and much knowledge.

Reflex Action. By F. FEARING. Pp. 350. London: Baillière, Tindall and Cox. 1930. Price 30s.

This volume, which is particularly interesting from the historical aspect, has been written by a psychologist as a study in the development of physiological psychology, but he does not attempt to present the reflex as the explanation of all the activities of the brain or mind, or to treat the subject only as a contribution to the history of psychology.

After an introductory chapter on the conception of voluntary and involuntary action of the Greek physicians and through the Middle Ages, he comes to Descartes, who in his description of animal automatism first recognized clearly that many of our activities are of a nature that would be now called reflex. The work of the early experimentalists is shortly reviewed, and the author then brings us to the more interesting speculations and experiments of the eighteenth century in which Croone, Whytt, Hartley, Blane, the Monros and other Englishmen took a large share. The work of Bell, Magendie, Marshall Hall, Flourens, Müller and others in the nineteenth century leads directly to the modern conception of reflexes, of the laws that control and integrate them, and the recognition of their fundamental importance in the activity of the body.

The investigations of Sherrington, Magnus and Pavlov are described, and finally the significance of the physiological conception of the reflex to various trends of psychology is considered.

The volume is well written, accurate as far as it can be controlled and unbiased in the presentation of facts and of the theories of the past. It contains much interesting information on the evolution of neurology and physiology.

Aphasia in Children. By ALEX W. G. EWING, M.A., Ph.D. Oxford University Press: Humphrey Milford. 1930. Pp. 152. Price 10s. 6d.

The literature of aphasia is enormous, but the subject of Dr. Ewing's valuable study has hitherto received very little attention. His painstaking investigations were into the apparent aphasia of children, in some of whom he found that the development of normal speech had been hindered by a remarkable form of partial deafness. The recognition of this lack of auditory acuity for sounds of higher vibration frequency was made possible by skilful and ingenious methods of examination, which are described in detail. Other children whom he investigated showed a congenital linguistic retardation different in kind from the aphasic disturbances of adults.

The book contains a valuable discovery and will be of great interest to otologists and to those concerned with the development of speech. In method of presentation it is admirable.

Die Hypophyse. Von A. EISELBERG, O. HIRSCH, O. MARBURG, J. NOVÁK, M. SGALITZER und E. A. SPIEGEL. Berlin: Urban und Schwarzenberg. 1930. S. 66. Price Rm. 3.50.

A year ago the Vienna Society of Medicine and Children's Diseases devoted a meeting to a discussion on the physiology and diseases of the hypophysis, and six of the contributions to this discussion are printed in this volume, which is therefore a valuable compilation of the state of our present knowledge of this subject. Spiegel deals with the anatomy and physiology of the pituitary, and especially with its functional relations with the tuber cinereum; Marburg describes in detail the clinical symptoms of hypophyseal diseases, mainly of tumours; Eiselberg and Hirsch write separately on the operative treatment of pituitary growths by the trans-sphenoidal route; Sgalitzer discusses the radiological therapy of tumours, and Novak the relations of the hypophysis to the sexual organs. The last paper, which is illustrated by photomicrographs, contains an interesting résumé of recent experimental work of this subject.

There is probably no other source in which such a complete and critical review of the physiology and diseases of the hypophysis can be found within the same space.

Étude sur les Narcolepsies. ALICE KYRIAGO-ROQUES. Paris: N. Maloine. 1930. P. 195.

Following the modern French tendency, the author deals with narcolepsy as a symptom due to some structural lesion or disease though it is not always possible to demonstrate it, rather than as a clinical entity. Consequently we find descriptions of narcolepsy as a complication of various organic and functional diseases of the nervous system and of disorders of the endocrine organs. Associated lesions have been most frequently demonstrated in the neighbourhood of the third ventricle and in the anterior part of the midbrain.

The nature of normal and pathological sleep is discussed in early chapters, and some recent experiments on the nervous mechanisms concerned in it are described. The histories of nine patients suffering with narcolepsy are published, and a very full and useful bibliography of the subject is included. Although the monograph adds little to our knowledge of narcolepsy, it will be a useful compilation to those interested in it.

Der Kopfschmerz und seine Behandlung. Von E. POLLAK. Leipzig und Wien: F. Deuticke. 1929. S. 158. Price Rm. 9.

As the recognition of the more common causes and the treatment of headache are the authors' aims, theoretical considerations as the causation and the origin or the pain in various conditions are reduced to a minimum. It is interesting, however, to find that the author believes the sympathetic nerve-fibres in the walls of the blood-vessels of the brain play a large part, and that the headaches which occur in association with disturbances of the circulation, intoxications and metabolic disorders are due to excitation or irritation of these fibres. The treatment of the subject is essentially practical; headaches are grouped according to their apparent cause, and the distinguishing features of each group and the most successful methods of treating them are described concisely and clearly. The book is evidently the work of an experienced clinician and will prove particularly useful to the practitioner and student.

Neuropsyche und Hirnrinde. Von N. E. ISCHLONDSKY. Berlin: Urban und Schwazenberg. 1930. Band I, pp. 328, price Rm. 20. Band II, pp. 356, price Rm. 22.

The first volume of this ambitious work is concerned with the conditioned reflex and its significance in biology, medicine, psychology and pedagogics. Dr. Ischlondsky claims for this study that it is a purely scientific discipline dealing only with measurable data and free from any trace of subjective concepts and speculative psychological tendencies. The investigations in this field have been carried out almost exclusively in Russia, and this book is a useful summary of the work of many physiologists, not elsewhere accessible.

In the second volume the conclusions about the activity of the nervous system are applied to the study of human behaviour. In the title, "Physiological Foundations of Depth Psychology, with especial reference to Psycho-analysis," the author's object is clear. How far he attains it is another matter. His enthusiasm is boundless; he says, for example, that the dynamics of the cerebral cortex during creative mental activity, the mechanism of consecutive and exact as well as of irrational thinking, of memory and will and moral conduct, the essential nature of culture and many more such hard problems are now for the first time completely solved; it becomes evident in reading the book that the claim is exaggerated. Many readers, however, will be stimulated by this bold attempt to clear up all the dark places by the application of a new point of view.

Psychopathology. By J. ERNEST NICOLE. London: Baillière, Tindall and Cox. 1930. Pp. xii + 203. Price 10s. 6d.

The first half of this book is intended to be a guide to the various schools of thought in psychology and psychiatry. The author is better at exposition than at critical appraisal; and many obscure and pretentious writers receive undeserved or disproportionate attention. The exposition, however, is clear and correct and covers a great deal of ground; naturally it does not pretend to be complete. Dr. Nicole appears to have limited himself to works available in English, if one may judge from the bibliography: this may account for his failure to refer to much recent work in Germany on the psychopathology of schizophrenia, and to do justice to some French and Swiss writers; there is, for example, no reference at all to the views of von Monakow, or of Mignard, Berze or Jaspers, and much of Janet's work is overlooked. Nevertheless, the author has read widely; some 500 books are listed in the bibliography.

In the second part of the book three essays are given. The first on "The Concept of the Ego in Psychiatry," and the third on "Psychopathology and the Herd Instinct," are lucid and interesting. The second on "Type Psychology" is poor; it is based on Jung's types and is rich in generalizations. The difficulties of writing such a book are great; Dr. Nicole has, however, successfully compressed much diverse material into a readable and coherent form.

Modern Psychotherapy. By EMANUEL MILLER. London: Jonathan Cape. 1930. Pp. 131. Price 5s.

Of all branches of medicine, there is none in which treatment is more dependent on theory than in psychiatry. This is especially true of that section of psychiatric practice that is concerned with the "minor psychoses" or neuroses. The divergent theories and the associated modes of treatment are described in this little book clearly and fairly, so that the general practitioner and the student, for whom the book is designed, can learn their main features without being deterred by verbiage and jargon or misled by the author's bias.

The analytic methods of Freud, Jung and Adler, suggestion in its various forms, and persuasion are described. There is a chapter on early treatment and prevention in which the difficult child and the person in the early stages of insanity are considered. A useful glossary of special terms is appended.

The scope of the book is necessarily limited by its size and purpose; the author disclaims any attempt at detailed exposition or critical analysis; the book is, therefore, compact and readable and not likely to give a false impression of finality.

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